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# FRACTURES OF THE ANKLE

## Analytic Historic Survey as the Basis of New Experimental, Roentgenologic and Clinical Investigations

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IN ANCIENT times lesions of the ankle were diagnosed chiefly as luxations, and early writers therefore always dealt with them in the sections on luxations. Not until after the middle of the eighteenth century were there traces in the literature of attempts to clarify the position of the malleolar fractures in relation to luxations of the ankle. It was especially in clinical works, particularly French and English, that attention was called to the serious nature of the fractures of the ankle and to the great difficulties connected with their treatment, and especially to the poor results which were often achieved, as it was impossible to prevent the treatment's leaving a greater or lesser degree of disability.

During the nineteenth century it was chiefly French scientists who worked at the problem of lesions of the ankle, and substantial results were attained by experimental-surgical research as well as clinically. Great progress was made with regard to the exploration of the pathogenesis, causation, symptoms, pathologic anatomy, prognosis and treatment of the lesions of the ankle, and, particularly, knowledge was increased of the malleolar fractures and their frequent occurrence in lesions of the ankle.

Yet it was not until the beginning of the twentieth century—soon after the introduction of the roentgenogram in clinical work—that the fractures of the ankle were interpreted as the central injuries, the primary lesions, in serious cases of lesions of the ankle.

According to Tanton,[1] a brief historical survey in the form of a condensed record of the contributions by earlier researchers to the explanation of the genesis, pathologic anatomy, classification, and clinical diagnosis of the lesions of the ankle will therefore naturally come under

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1. Tanton, J.: Fractures, Paris, J.-B. Baillière et fils, 1915-1916.

three headings: the clinical period, the experimental period and the roentgenographic period.

## THE CLINICAL PERIOD

Hippocrates [2] (about 300 B. C.) gave a rather detailed account of the lesions in the region of the ankle and stated that the crural bones in the talocrural joint may luxate inward, outward, forward and backward and that the luxations may be found together with fractures in the distal end of the crural bones and sometimes in connection with lesions of the skin (compound fractures).

In the treatment he distinguished between luxations with and without lesion of the skin. In the former case reposition must not be performed, as the patient will then die within seven days.

A. Cornelius Celsus [3] (first century) dealt with lesions of the ankle in a less detailed way than did Hippocrates, but he stated that the talus will frequently luxate inward and outward and that it is important to reduce the talus well under the tibia for the purpose of weight bearing.

The writers Oribasius, Paulus Aeginata, Albucasis, Ruggiero Frugardi, Rolando Capelluti, Guy de Chauliac, Johann Scultetus (Ulm) and Laurentius Heister did mention these injuries, but at the times when their works were written research had not reached a close examination and explanation of the diseases of bones and joints, so that their literary works do not give any details about lesions of the ankle beyond what Hippocrates stated.

Jean-Louis Petit [4] (1723) mentioned, in contrast to Hippocrates, that the talus and the foot are the luxating parts, which may luxate inward, outward, forward and backward.

In his opinion luxation in the talocrural joint will only be found in connection with malleolar fracture or diastasis between the malleoli. He often found fractures in the distal end of the fibula, but most frequently in the medial malleolus in connection with luxation.

Petit was aware of the difficulty of treating patients with luxation so as to obtain complete function and remarked that his contemporaries complained that these injuries result in limping and deformity. In his opinion the most important measure to avoid these sequelae is careful reposition. Petit pointed out that sprain of the foot may be even more serious than luxation and that, if it is neglected, it may result in inflammation of the tendon sheaths and periarticular tissues, formation of abscesses, deformed leg or even death, if skilful treatment with absolute rest is not instituted.

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2. Hippocrates: Opera omnia Lugd. Bat., apud D. A. et A. a Gaasbeeck, 1665, vol. 1-2; English translation by E. T. Withington, London, 1928.

3. Celsus, A. Cornelius: De medicina libri octo, Lipsiae, B. G. Teubneri, 1859.

4. Petit, J. L.: Traité des os, Paris, C.-E. Hochereau, 1723.

J. G. Duverney [5] (1648-1730) was, like Petit, aware of how serious a lesion of the ankle is, especially if it is left untreated. He presumed that patients with violent luxation fractures can be cured only by primary amputation.

Jean-Pierre David [6] (1771) in his prize essay to l'Académie Royale de Chirurgie in Paris under the pseudonym of "Basylle," was the first who tried to explain the origin of indirect fractures. He believed that they are caused by a violent forced movement of one bone toward another, by which the latter is fractured (*contre-coup*). Thus fracture of the distal end of the fibula is said to be caused by a violent outward movement of the foot by which the fibula is pressed upward by the talus. As the fibula is held back by the ligaments and as the distal articular surface of the tibia prevents the talus from rising proximally, the distal end of the fibula will be forced outward by the pressure exercised by the talus and by the action of the peroneal muscles and will break at its weakest point, i. e., just proximally of the lateral malleolus. However, David did not consequently follow his theoretic explanation in his treatment of patients.

W. Bromfeild [7] (1773) criticized the doctors of his day who regarded the fibular fracture as comparatively insignificant, as no importance was attached to the fibula in transmitting the weight of the body from the femur to the foot. For this reason the doctors were not interested in diagnosing the fibular fracture when they could ascertain fracture in the distal end of the tibia, and in many cases it was therefore an immense disappointment when the dressing was removed and they found a severe deformity in the ankle region with the foot turning outward in spite of the healed tibial fracture. The deformity is due to an undiagnosed fracture distally in the fibula. Like Petit he emphasized the dangerous nature of sprains. He called vigorously for care in diagnosis and reposition of the fibular fracture, which clearly proves the importance which he attached to it in cases of luxation, and his application of compresses proves his correct interpretation that the malleolar fragment gives way laterally in the distal end and approaches the tibia proximally (fig. 1).

Percival Pott [8] (1775) stressed the great importance of the fibula as a support in the ankle region in spite of its slender structure as compared with the tibia. Without the support of the fibula, he said, the body cannot be held erect, since abnormal movements of the foot may be expected at any moment.

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5. Duverney, J. G.: Traité des maladies des os, Paris, De Bure l'aine, 1751.

6. David: Mémoire sur les contre-coups dans les différentes parties du corps autres que la tête (Pris de l'academie royale de chirurgie), 1771.

7. Bromfeild, W.: Chirurgical Observations and Cases, London, T. Cadell, 1773.

8. Pott, P.: The Chirurgical Works, London, Hawes [and others], 1775, p. 664.

He was the first who stated in detail the pathologicoanatomic findings in a certain type of fracture in the ankle region. In this a fracture of the fibula was found 2 to 3 inches (5.1 to 7.6 cm.) above the distal tip of the fibula, rupture of ligament at the medial malleolus and partial dislocation or rather luxation of the talus laterally (fig. 2).

He observed that the proximal end of the fibular fragment approaches the tibia while the malleolar end is displaced laterally, and noted thus a dislocation which Bromfeild had pointed out was present in patients and to which he directed his treatment.

Pott illustrated this type of fracture in a sketch by which Pott's fracture is now easily recognized by roentgenography, and he said that this type of fracture may be difficult to treat, and that in any case it calls for great skill to do so, if the fracture shall not later on cause deformity or painful extremity, which in turn may require amputation or use of splints and a wooden leg for the rest of the patient's life.

Fig. 1.—Traction apparatus used at the end of the eighteenth century.

Accordingly Pott attached great weight to a good reposition and managed to perform this far more easily than his predecessors, introducing reposition in "semiflexion"; i. e., the extremity is held half flexed in the hip joint and knee joint, by which the muscles are relaxed to the greatest possible extent and thus the least possible counteraction to the reduction is caused. By means of strips of adhesive tape over the lateral malleolus around the planta and up on the medial side of the crus, and by placing the injured extremity in semiflexed position he tried to secure retention (fig. 3).

Fabre[9] (1783) pointed out, like Petit and Bromfeild, how serious an affliction sprain and luxation in the ankle joint is, but emphasized also that the fibular fracture accompanying the sprain is frequently left undiagnosed.

9. Fabre, P.: Recherches sur différens points de physiologie, de pathologie et de thérapeutique, Paris, T. Barrois, 1783.

He cited such cases, in which the fracture was not ascertained in principle, which resulted in deformity with external rotation of the foot, for which patients sued the doctor for damages.

Heinrich Callisen [10] (1788) in his famous work on surgery discussed the lesions of the ankle in the section "Luxatio pedis seu ossis tali."

He ascertained in cases of outward luxation fracture of the lateral malleolus or rupture of ligament and planta turning inward. In cases of inward luxation he found fracture of the medial malleolus and planta

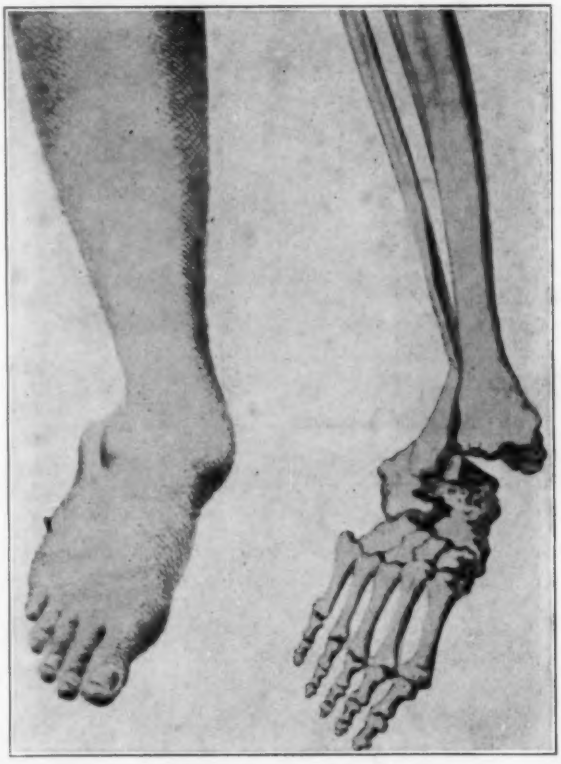

Fig. 2.—Pott's illustration of the fracture which bears his name. (Surely there have been marked syndesmotic rupture and diastasis which, however, do not appear from the illustration.)

turning outward. These explanations about fractures of the ankle correspond to what more recent writers termed adduction and abduction fractures. In cases of forward and backward luxation Callisen stated that the heel region is contracted and extended respectively.

10. Callisen, H.: Principia systematis chirurgiæ hodiernæ in usum publicum et privatum adornata, Hanniæ, Proft, 1788-1790.

Anthelme-Balthasar Richerand[11] (1803) turned his attention to David's theory about the origin of indirect fractures in the ankle region and tried to associate this mechanism of fracture with the normal curvature of the distal end of the fibula. This curvature is formed because the talus, whenever the weight of the body rests on the foot, reacts on the lateral malleolus, so that it is forced upward and outward. By this the tibiofibular ligament exercises a considerable pull at the supramalleolar-fibular region. In the early part of life the bones curve

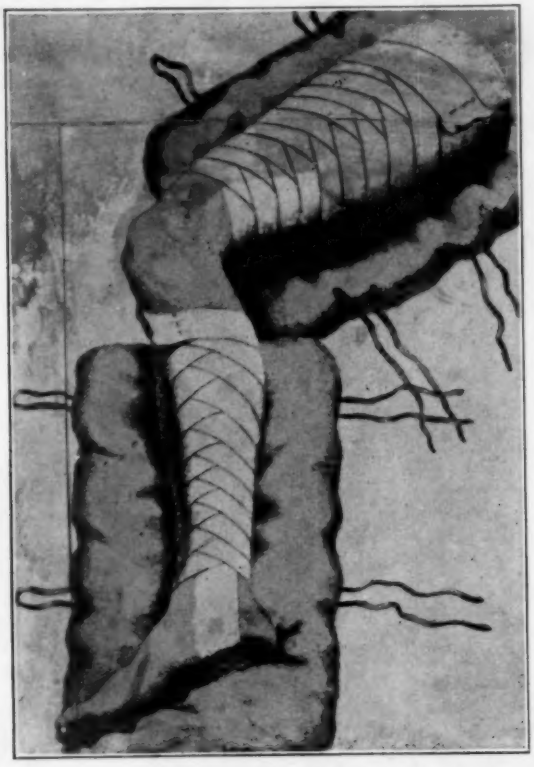

Fig. 3.—Pott's illustration of the dressing of fracture of the ankle and placing the leg in "semiflexion."

in this place but straighten again when the weight does not rest on the foot. In time the curvature gradually becomes manifest owing to the action of the talus. By forced abduction the action may exceed the physiologic limit and produce a fibular fracture proximal to the lateral malleolus.

11. Boyer, A.: Leçons sur les maladies des os, arranged by A. Richerand, Paris, Migneret, 1803, vol. 1, p. 294.

Alexis Boyer[12] (1803) was, however, the first who tried to form a theory about the origin of fractures of the ankle, indicating more concisely and distinctly than did David and Richerand how these fractures may arise.

The significance of Boyer's statements is that he, like Petit, supposed that there will always be malleolar fracture or lesion of ligament in luxation in the talocrural joint, and he presented the first attempt at theoretically explaining the genesis of the fractures accompanying the luxations. He did not include in his reflections on fibular fractures and luxations in the talocrural joint such observations as his predecessors had made and stated from clinical work or from autopsy.

### THE EXPERIMENTAL PERIOD

G. Dupuytren[13] (1777-1835), who was a pupil of Boyer, subjected the lesions of the ankle to a close study; he carefully went through the literary works from the time prior to his own, learning something from them (in contrast to Baron Boyer), and then continued his studies of these injuries in an independent way, partly by experimental-surgical investigations and partly by clinical research.

Dupuytren adopted in principle Boyer's theory of the origin of the fibular fracture by adduction and abduction of the foot.

He was the first to undertake experimental-surgical investigations by producing fractures of the ankle in cadavers. According to his experimental-surgical investigations, Dupuytren explained the genesis of the malleolar fractures, and even if he still thought that the fractures are produced by forced adduction or abduction in conformity with Baron Boyer's theory, there is nevertheless such a difference between Boyer's interpretation of what happens in the two movements of the foot and that of Dupuytren that the latter's theory must be taken as quite independent of that of Boyer.

Dupuytren performed his surgical experiments as follows: The foot is fixed distal to the malleoli, and the crus is moved medially and laterally. By this procedure the ligament on the malleolar side is relaxed on the side to which the crus is moved while the ligament on the opposite side is tightened and extended so that a sprain is produced.

If the movements of crus are performed quickly and with great force, the outward movement (abduction of foot) will result in (1) fracture of the medial malleolus and (2) fracture of the distal end of the fibula, and the inward movement (adduction of foot) will result in (1) fracture of the distal end of the lateral malleolus and (2) fracture

12. Boyer, A.: Traité des maladies chirurgicales et des opérations qui leur conviennent, Paris, Ve. Migneret, 1814.

13. Dupuytren, G.: Leçons orales de clinique chirurgicale, ed. 2, Paris, Germer-Baillière, 1839, vol. 1, p. 378.

of the medial malleolus (note what Dupuytren understands by adduction and abduction). Yet Dupuytren did not find the latter stage of fracture by adduction and abduction in his experiments, but, on the contrary, in patients. Fracture in the distal end of the fibula could thus be produced both by adduction and abduction. By adduction the fibular fracture is the primary lesion and by abduction the secondary one.

It is now seen how Dupuytren's theory, which he thought that he had proved, partly by his experiments and partly by his clinical observations, deviates from Baron Boyer's hypothesis, according to which the fibular fracture should be the primary lesion both by adduction and by abduction. Dupuytren's theory also differs from that of Boyer in that it mentions and comprises fractures of both malleoli.

Dupuytren thought that the fibular fracture is much rarer than the tibial fracture, the ratio of incidence being 1 to 3, but he pointed out that many fibular fractures are misinterpreted and erroneously presumed to be luxation or sprain of the ankle joint. He thought that fracture of the distal end of the fibula is a much more frequent occurrence than was generally presumed at his time.

Dupuytren made a distinction between direct and indirect fibular fractures. In his opinion the former are of slight clinical significance, partly because they are rare and partly because they do not require any treatment. In agreement with the statements of the previous writers he thought that the indirect fractures are of a far more serious nature, as they will disable the patients for life and in the days following the accident they will create critical situations if the injury is not disclosed at once and subjected to an effective treatment. Also Dupuytren was struck by the fact that a slight cause may give rise to this serious affliction.

In one group of patients suffering from fracture of the ankle he described the position of the foot thus: The lateral edge of the foot rises and the medial edge sinks, the dorsum pedis faces directly proximal and the planta a little upward. The rounded upper surface of the talus faces the internal malleolus and sometimes forms a prominence here as an inward luxation of the talus is found. The upper end of the lateral malleolar fragment approaches the tibia, for which reason the skin at the seat of the fracture will be retracted (*coup de hache*). The foot is displaced laterally, and the tibial axis will, if extended, fall on or inside the medial edge of the foot. This lateral displacement of the foot is in Dupuytren's opinion the only dislocation which necessarily appears, and it is the more conspicuous when the fracture is near the distal end of the fibula or when the patient has tried to walk after the accident.

This description applies to abduction fractures, and this finding is the commonest in spite of the fact that Dupuytren thought that six tenths of the fractures of the ankle are produced by adduction while only three-

tenths should be produced by abduction. Dupuytren explained this discrepancy by stating that even if the fracture is produced by adduction, the muscular force or the patient's attempts at walking after the trauma will at once move the foot laterally, so that the foregoing description of the position of the foot will also apply to a great number of the cases which have been produced by adduction.

Dupuytren himself believed that his patients with abduction fractures were suffering from the type of fracture which had been presented and described by Percival Pott.

In another group of patients Dupuytren described the position of the foot thus: The foot is turned inward with luxation of the talus outward under the lateral portion of the ankle. The medial edge of the foot turns upward, the lateral downward, and the planta inward so that the foot resembles a congenital clubfoot. This position is chiefly found in such cases of fracture as have been produced by a slight external cause, such as a false step or a stumble, and when the line of fracture is situated more distally—2½ inches (6.4 cm.) or less above the tip of the lateral malleolus. Dupuytren regarded this position of the foot as peculiar and unusual and believed that it is due to the obliquity of the generally concomitant fracture in the base of the medial malleolus, but otherwise admitted that he could not explain its genesis and that he did not know its actual nature. He was yet inclined to think that this fracture also is produced by forced abduction of the foot.

Later it will be seen how this clinical picture corresponds to a type of fracture the mechanism and nature of which are—partly—explained by Maisonneuve.

Dupuytren regarded the fibular fracture as complicated when it is accompanied by a fracture of the medial malleolus or rupture of its side ligament.

In one half of Dupuytren's cases the fibular fracture was situated less than 2 inches above the tip of the malleolus. In nine tenths of the cases there were displacements of various kinds. In seven tenths there were lateral displacements.

With effectiveness equaling the care and energy with which he worked to explore the genesis of the malleolar fractures, to classify them and to explain their clinical picture, Dupuytren described his method of reposition and his splint, in strictly logical agreement with the results which he achieved by his experimental-surgical investigations and his clinical considerations.

He performed reduction by extending the foot, which was then adducted, supinated and plantar flexed in order to remove the dislocation of the foot and in order to move the fragment of the lateral malleolus in distal-medial direction by means of the intact ligaments between this and the talus-calcaneus. His splint was designed for the retention of this position of the foot (fig. 4).

Dupuytren was the first who clinically observed and described central luxation of the talus. In this he found fracture of the fibula, distal rupture of the ligaments between the tibia and fibula, displacement of the talus and the malleoli in fibular direction, and 2 inches proximal dislocation of the trochlea tali along the lateral surface of the tibia up between this bone and the fibula.

It is this lesion of the ankle which justly bears Dupuytren's name. In the course of time Dupuytren's name was also attached to other forms of fractures of the ankle. Thus, the form of fracture which was first described by Pott was called *fracture, Dupuytren type,* and the forms of fractures which were later described and experimentally produced by Maisonneuve [14] and Tillaux,[15] respectively, were called *fracture, Dupuytren basse.*

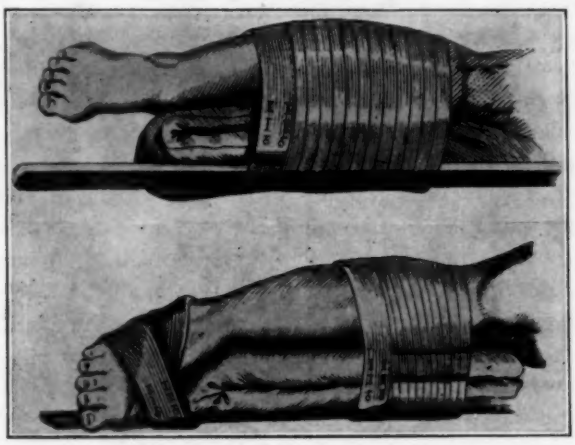

Fig. 4.—Dupuytren's splint. Note the position of the foot after reduction.

The attachment of Dupuytren's name to these forms of fractures is justified by his description of two different clinical pictures of fractures of the ankle and not by his knowledge of the actual nature and genesis of these types of fractures. For he supposed that they are all fractures of the kind which Pott had described and therefore treated them all in the same way. In literary works right up to the present day this has caused much obscurity and confusion in the field of fractures of the ankle, because the designations "Pott's fracture" and "Dupuytren's fracture" are used partly as terms which comprise all supramalleolar fractures and are synonymous, and partly as designations for groups of fractures which are thought to be widely different.

14. Maisonneuve, J. G. T.: Recherches sur la fracture du péroné, Paris, F. Loquin & Cie, 1840; Arch. gén. de méd. **7**:165 and 433, 1840.

15. Tillaux: Recherches cliniques et expérimentales sur les fractures malléolaires (Rap. de Gosselin), Bull. Acad. de méd., Paris **1**:817, 1872.

Charles Bell [16] (1809), wrote on fractures of the ankle in the same period as Dupuytren.

John Howship [17] (1816) reported observations of sequelae of fracture of the distal end of the fibula. He presumed that the condition is caused by the external rotation of the foot, by which the weight of the body affects the ligaments of the medial malleolus to such a degree that they cannot resist the pressure. He was presumably the first to report precisely and to try to explain the valgus position of the talus after a fracture of the ankle. He recommended an appliance to support such a deformity of the foot.

Astley Cooper [18] (1823) treated the luxations in the talocrural joint in a large work. What is particularly interesting in this is his pathologicoanatomic findings with regard to fractures of the bones in the ankle region in various forms of luxation.

His statements are so detailed and extensive that it has never since been possible to ascertain a form of ankle fracture which has not been found and described by him. (Yet the pronation-dorsiflexion fracture forms an exception. This is discussed in a subsequent paper.)

Cooper presumed, like Hippocrates, that it is the tibia or more precisely the crural bones that luxate and not the foot. He mentions luxation of the tibia inward, outward, forward and backward, and in addition a fifth form of luxation with the talus pressed up between the crural bones. This luxation was originally described by Dupuytren, but Cooper expressed the opinion that it is only an aggravation of inward luxation.

Inward luxations of the tibia are most frequent. Thereby the foot is displaced laterally, and its medial edge rests on the support. In the skin proximal to the lateral malleolus there is a considerable depression (Dupuytren's *coup de hache*), and here the crepitus of the fracture is noted 3 inches (7.6 cm.) above the tip of the malleolus. From the lower lateral part of the tibia where this bone is attached to the fibula by ligaments a fragment is torn off, which remains attached to ligaments and the fibula.

In forward luxation the distal articular surface of the tibia is found resting on the upper surface of os naviculare and collum tali. The fibula is fractured 3 inches above the tip of the lateral malleolus, and the proximal fibular fragment is displaced forward simultaneously and in normal relation to the tibia. The fibular fracture runs obliquely upward

16. Bell, C.: A System of Operative Surgery, London, Longman [and others], 1807-1809.

17. Howship, J.: Practical Observations in Surgery and Morbid Anatomy, London, Longman [and others], 1816.

18. Cooper, A. P.: A Treatise on Dislocations and on Fractures of the Joints, London, The Author, 1823.

and backward through the portion of the bone which is part of the distal tibiofibular articulation. The deltoid ligament is partly torn. The articular capsule is torn in front.

In partial forward luxation of the tibia there is a lesser forward displacement of the tibial articular surface. On a specimen which Cooper received from one of his colleagues, and which came from a patient who had suffered from such a luxation, the distal articular surface of the tibia was separated by a fracture. The anterior part of the articular surface rested on the dorsal part of the collum tali where an articular surface had developed, while the posterior part of the articular surface rested against facies superior trochleae tali. There was also a high fibular fracture.

Cooper himself had seen such a fracture, which he could not reduce, and the patient had to walk on crutches for the rest of his life. It seems to be the first publication of a case of fracture of the dorsal part of the tibia which is reported here.

In outward luxations of the tibia there are said to be extensive lesions of ligaments and soft parts in connection with fractures of the ankle. The foot turns inward with the lateral edge downward. The medial malleolus has an oblique fracture, and sometimes a piece of the adjacent tibial diaphysis adheres to this malleolar fragment. The fibula is fractured in a number of splinters. The three ligaments at the lateral malleolus remain intact in most cases, but if the fibula is not fractured they will rupture.

The pathologicoanatomic finding which is reported in inward luxation corresponds to Pott's fracture with fibular fracture 3 to 3½ inches (7.6 to 8.9 cm.) above the tip of the malleolus, and to the clinical description of Dupuytren's abduction fracture, while the pathologicoanatomic picture which is described in outward luxation exactly corresponds to that which Dupuytren's theory gives of adduction fracture.

The pathologicoanatomic observations in forward luxation of the tibia and partial forward luxation will be discussed later in connection with the results of Maisonneuve's [14] experiments.

I. G. Maisonneuve [14] (1840) carefully reviewed the theories of fracture of the ankle as they had been set forth by Baron Boyer and Dupuytren, and expressed the belief that Boyer's explanation of the genesis of the fractures by adduction or abduction is nearest the true facts and is most clearly and precisely set forth.

Nevertheless, he himself was of the opinion that most fractures in the ankle region do not agree with these theories. He stated the belief that especially the fractures of the ankle in which the fracture of the fibula is situated around and just above the ankle joint and which are most frequently accompanied by luxation of the foot—the very form of ankle fracture which is most feared by the clinicians and the writers

who have treated that subject—must have another mechanism of fracture than that described by Baron Boyer and Dupuytren.

Maisonneuve performed experimental surgical investigations in order to throw light on this obscure point and in order to determine the great importance which he attached to external rotation of the foot for the production of fracture of the ankle.

With regard to the movements of the foot Maisonneuve stated that practically no adduction or abduction movement is possible between the talus and the malleoli. The system of taut ligaments from the foot to the malleoli maintains the close connection between the articulating surfaces of the talus and the malleoli and prevents side movements of the talus in the malleolar fork. It is, on the contrary, the task of the malleoli to prevent sidewise displacement of the talus. A movement which tends to separate the malleoli will therefore affect only them and not the side ligaments.

The sidewise movements of the foot can take place only between the talus and the calcaneus, and adduction of the foot in the articular connection between these two bones is possible to an essential extent, particularly when adduction is combined with rotation of the foot around its longitudinal axis without this movement's influencing the malleoli. If, on the contrary, the foot is abducted, it is instantaneously transformed into an inflexible tube, a lever, by which the pressure on the medial side of the anterior part of the foot (external rotation) is at once transmitted to the malleoli.

By external rotation of the foot the malleoli will therefore be traumatically affected when the pressure of the external rotation has reached a certain value.

Maisonneuve imitated Dupuytren's [13] experiments with forced abduction of the foot and produced rupture of the ligamentum malleoli medialis, but never fracture of the lateral malleolus such as should occur according to Dupuytren.

Nor did Maisonneuve observe any contact between the calcaneus and the tip of the lateral malleolus such as Baron Boyer had stated should be the case in the production of the abduction fracture in the lateral malleolus.

By forced adduction he always produced fracture of the lateral malleolus in conformity with Dupuytren's and Boyer's [12] theories. Here the fracture is invariably transverse and is found in the distal half of the malleolus itself and never in the distal end of the fibula. By continued adduction the fragment may be displaced medially, but it is reduced by abduction of the foot.

After this Maisonneuve did not agree with Dupuytren, who had maintained that the adduction fracture occurred most frequently, that it had its seat proximal to the ankle joint, and that it had a tendency to lateral displacement by abduction.

Maisonneuve found, on the other hand, that the fragment can be dislocated laterally by external rotation of the foot.

By external rotation of the foot Maisonneuve then produced two widely different fractures in the fibula.

When the ligaments between the tibia and fibula are intact, an oblique spiral fracture is produced in the distal end of the fibula. The fracture line is invariably found with the same course and in the same place in the fibula, and reaches up to nearly 2 inches (5.1 cm.) above the tip of the malleolus, the direction being posterior-anterior, superior-inferior and lateral-medial. This fracture is most frequently found and is not accompanied by lesions of ligaments and aponeuroses. By continued external rotation the ligamentum malleoli medialis will be torn and sometimes the medial malleolus will be fractured. The fibular fracture is always the primary lesion.

Maisonneuve presumed that the fracture occurs in the distal part of the fibula because the lever formed by the anterior part of the foot is 12 to 15 cm., whereas the talus held between the malleoli is only 3 cm. and thus represents a shorter lever, because the lateral malleolus is the longest and because the fibula is the weakest bone.

Maisonneuve illustrated the mechanism in the fracture experiment as follows: Two books are placed on edge side by side, and the short part of a stick is pushed in between the books. By moving the free and longer end of the stick sideways the book on the side to which the stick is moved is displaced. This corresponds to exposure of the lateral malleolus to the greatest pressure by external rotation of the foot, so that a fracture occurs in the distal end of the fibula.

When the ligaments between the tibia and the fibula are torn, a greater or lesser separation of the two bones will take place distally, so that a "diastasis" appears. If the external rotation is then continued, a fracture is produced in the proximal part of the fibula. It is this type of fracture which bears Maisonneuve's name. Later on in this work it will be shown that the oblique spiral fracture of the distal end of the fibula is of far greater importance clinically, and that it would be more appropriate for this to bear Maisonneuve's name.

Maisonneuve did not state whether the foot is held supinated, pronated, plantarflexed or dorsiflexed during the forced external rotation of the foot.

The position of the foot after the production of the oblique spiral fracture was stated by Maisonneuve to be as described by Dupuytren in some cases of fractures of the ankle in which the lateral edge of the foot was turned downward, the medial edge upward, and the planta inward. Maisonneuve ascertained that all these phenomena disappear as soon as the foot is subjected to internal rotation. The pathologico-anatomic picture fully corresponds to that given by Cooper for forward luxation of the tibia.

After this Maisonneuve himself would not deny or reject the theories set forth by Baron Boyer and Dupuytren that fractures in the ankle region may occur in the manners indicated in their theories, but he was of the opinion that his own experiments proved that fractures in the ankle region may also occur otherwise, namely by the mechanism stated by himself, which is intended to explain that most fractures of the ankle are produced by external rotation of the foot.

M. T. Boyer [19] (1845) divided the malleolar fractures into two main groups: (1) supramalleolar fractures (fractures near the ankle joint in the parts of the crural bones which are in ligamentous connection with each other) and (2) bimalleolar fractures. Boyer saw many of the latter category, and he was surprised that they did not excite greater interest, as they are fractures which involve the ankle joint and which from a clinical point of view are of greater importance than for example the fractures of the crus, leaving as they do greater deformity than these (flatfoot).

Malleolar fractures as such were here mentioned for the first time in the literature. He refused to believe that these fractures are produced by the mechanism indicated by the theories of Boyer, Dupuytren and Maisonneuve, and presumed that something else must happen locally at the same time.

Bonnet [20] (1845) performed experimental investigations with a view to ligamentous and capsular lesions in the talocrural joint and in the joints of the foot by filling the joint cavities by injection and then making forced movements of the foot. In these experiments he found that the adduction and abduction movements take place in the joint between the talus, calcaneus and os naviculare, and between the calcaneus and the os cuboideum. If these movements are carried to the extreme, they will cause sprains and fractures.

By adduction he produced (1) fracture of the lateral malleolus in the distal half or tearing of the ligaments from its tip and (2) fracture at the base of the medial malleolus and in the adjacent part of the tibial diaphysis.

The latter fracture occurs only when the whole foot is fixed during the adduction and when, at the same time, a pressure is exercised on the crus in the distal direction.

Bonnet was thus the first who by forced adduction experimentally produced a secondary fracture in the medial malleolus, which according to Dupuytren's theory should occur, and which Dupuytren had found in patients.

By abduction a longitudinal fracture of calcaneus is produced when the foot is fixed by this bone in a vise, and the crus is moved laterally.

19. Boyer, M.: Traité des maladies chirurgicales, ed. 5, Paris, Labé, 1844-1849.

20. Bonnet, A.: Traité des maladies des articulations, Paris, J.-B. Baillière & Germer-Baillière, 1845.

When the foot is fixed by the anterior part, and the crus moved laterally, rupture of ligaments between the tarsus and crus will occur. If, on the other hand, the foot is fixed at both the medial and the lateral edges, a primary fracture in the medial malleolus will quickly be produced by an outward movement of the crus under pressure in its longitudinal direction. By this experimental arrangement a secondary fracture is produced in the lateral malleolus, the seat of which varies.

Thus Bonnet experimentally produced fractures in both malleoli both by adduction and by abduction, and the fractures occurred in the order indicated by Dupuytren.

The primary lesion of the adduction fracture of the lateral malleolus is found in its distal half, just as Maisonneuve had ascertained.

Malgaigne [21] (1847) gave his view of the lesions in the ankle region in his treatises on fibular fractures, supramalleolar fractures, malleolar fractures and luxations in the talocrural joint. He stated that the fibular fractures are most frequent in the ages between 25 and 50 years, four times as frequent in males as in females.

Malgaigne, reflecting on the genesis of all these different fractures of the ankle, said that even the most comprehensive theory framed according to experiments on cadavers cannot include all the cases because of their great variety. His arguments against the experimental-surgical results will be stated here because they are essentially the same as have been used by later authors (Quénu,[22] Destot,[23] and Svend Hansen [24]) when they dissociated themselves from experimental surgery. Malgaigne said that if one considers the greatly varying circumstances under which the fractures occur (when one strikes the foot against a stone, or, when walking, places it in a small depression or on an elevation in the ground, or has one foot slip away from the other, or has the foot held fast in a certain position while the body falls to one side, or stands on the toes, on the heel or on the medial or lateral edge of the foot while the anterior part of the foot is turned inward or outward, with the crus in either extended or flexed position), it will be understood that it is impossible to introduce all factors into experimental surgery. To all these elements should also be added the effects of the

21. Malgaigne, J. F.: Traité des fractures et des luxations, Paris, J.-B. Baillière, 1847-1855; Une revue de la clinique de M. le professeur Dupuytren durant le mois d'août, Gaz. méd. de Paris, 1832, p. 647.

22. Quénu, E.: Du diastasis de l'articulation tibiopéronière inférieure, Rev. de chir., Paris **35**:897, 1907; **36**:62, 1907.

23. Destot, E.: Diastasis et fracture des malléoles, Rev. de chir., Paris **27**: 279, 1907; Traumatismes du pied et rayons X, Paris, Masson & Cie, 1911; A propos des fractures du cou-de-pied, Rev. de chir., Paris, **45**:439, 1912; La troisiéme malléole: Fracture marginale postérieure, Lyon chir. **9**:256 and 391, 1913.

24. Hansen, S.: Om ankelbrud disputats, Copenhagen, P. Madsens Boghandel, 1919.

various positions and the weight of the body, which may also influence the production of the fracture.

In his division Malgaigne excluded these experiments, the value of which in his opinion is problematic, and kept to what practical facts, the statements of the patients that they had contracted the fracture of the ankle either by forced adduction or by forced abduction of the foot, seemed to show him.

In the former case the weight of the body rests on the lateral edge of the foot at the moment of trauma, by which the foot at the same time turns a little inward, and produces a primary fracture of the lateral malleolus and a secondary one of the medial malleolus (*"fractures par adduction"*). In the latter case the medial edge of the foot carries the weight of the body at the moment of trauma, and when at the same time the foot makes a forced abduction movement, the anterior part points a little outward. In this case a primary fracture of the medial malleolus and a secondary one of the lateral malleolus occurs (*fractures par abduction*).

Malgaigne made no mention of Bonnet's [20] work, or the results clearly set forth in it, which showed how and in which order the malleolar fractures occur by adduction and which malleolus primarily fractures by abduction.

Nor did he seem to have noticed that the oblique spiral fracture in the distal end of the fibula, which Maisonneuve produced experimentally, might have some connection with the oblique fracture found by Cooper [18] in the distal end of the fibula by forward luxation of the tibia.

By inward luxation of the tibia he gave—like Cooper, but more clearly than this writer—a pathologicoanatomic picture which corresponded to Pott's fracture, as fracture or rupture of ligaments at the medial malleolus, fibular fracture 3 inches or more above the tip of the lateral malleolus and lateral displacement of the talus were found. Furthermore, he observed detachment of the ligamentum interosseum tibiofibulare with avulsion of a bony shell from the tibia laterally. Pott did not say anything about the latter point in his description of his type of fracture, even though he emphasized the great significance of the ligaments for the maintenance of the normal physiologic position of the articular surfaces.

Malgaigne performed as good a reduction as possible and placed the extremity in a plaster cast while pressure was exercised on the malleoli.

P.-C. Huguier [25] (1847) performed experiments on cadavers to find out the mechanism by which lateral and dorsal luxation of the talus occurs. He placed the cadaver on its back with extended lower extremity, which was fixed to the support. The anterior part of the foot was held

25. Huguier, P.-C.: Mémoire sur les luxations du pied considerées en général, Paris, 1848; Union méd., Paris **2**:120, 1848.

dorsiflexed, and then rotated outward with great force, by which detachment of the ligamentum malleoli lateralis anterius and of the ligamentum interosseum tibiofibulare was produced, so that a distal separation between the tibia and fibula, fracture of the fibula 3 inches or more (twice in the proximal part of the fibula) proximal to the lateral malleolus and rupture of the ligament from the medial malleolus occurred.

By external rotation of the foot Huguier noted that the talus tends to turn in the malleolar fork, so that the posterior part of the medial surface of trochlea tali presses against the articular surface of the medial malleolus, while the anterior part of the lateral surface of the trochlea tali presses against the articular surface of the lateral malleolus.

After the rupture of the ligament distally between the tibia and fibula the talus, during rotation around a vertical axis, is displaced laterally. The lateral malleolus is pushed outward and dorsally by the talus, turning around its own axis until the fibular fracture occurs. The talus then luxates further laterally and somewhat dorsally, and the lateral malleolus also is further displaced laterally and dorsally during increasing rotation, while the separation increases correspondingly.

Huguier did not state in which position the foot was held during the forced external rotation.

It is seen that Huguier experimentally produced a fracture of the ankle of the Pott type, the pathologicoanatomic picture of which is identical with that which according to Cooper and Malgaigne was found by inward luxation of the tibia.

Huguier carefully pointed out that a considerable separation occurs (of this Pott said nothing), but, unlike Cooper and Malgaigne, he did not observe avulsion of bone from the lateral part of the tibia.

Laborie [26] (1866) reported an autopsy in which he found a fibular fracture 5 cm. above the lateral malleolus and a vertical fracture anterolaterally in the tibia. The fragment (2 cm.) was anchored to the fibula by the ligamentum malleoli lateralis anterius.

R. von Volkmann [27] (1875), on operation in two different types of fractures of the ankle, found a fragment torn from the anterior part of the tibia. In a case of compound fracture the foot was in extreme valgus position. At operation—resection—in this case, fracture in the apical part of the medial malleolus, fracture of the fibula 3 inches above the lateral malleolus and also a fracture at the articular surface of the tibia were found. The fracture line had a longitudinal course in the sagittal plane, so that a wedge-shaped fragment 7 cm. long had been

26. Laborie: Fractures multiples de l'omoplate, de la clavicule, de l'humerus droits, avec luxation de l'épaule et pseud-arthrose du corps de l'humerus, Bull. Soc. de chir. de Paris (1866) **7**:297, 1867.

27. von Volkmann, R.: Beiträge zur Chirurgie, Leipzig, Breitkopf. u. Hartel, 1875, p. 105.

torn off the anterior lateral part of the tibia (fig. 5, left). The fragment was anchored to the fibula by the ligaments. No fracture of the posterior lip of the tibia was noted.

The mechanism of fracture in this case was in von Volkmann's opinion as follows: By pronation and abduction the lateral malleolus is pushed violently upward and outward, whereby a fibular fracture occurs 3 inches above the malleolus. As the trauma continues, the ligaments between the tibia and fibula are strained to the extreme, and now they either rupture (most frequent) or, if they do not, an avulsion of the part of the tibia to which they are attached will occur.

Whether the ligaments are ruptured, or they are torn from the tibia with a bony shell, a "diastasis" is produced either between the tibia and

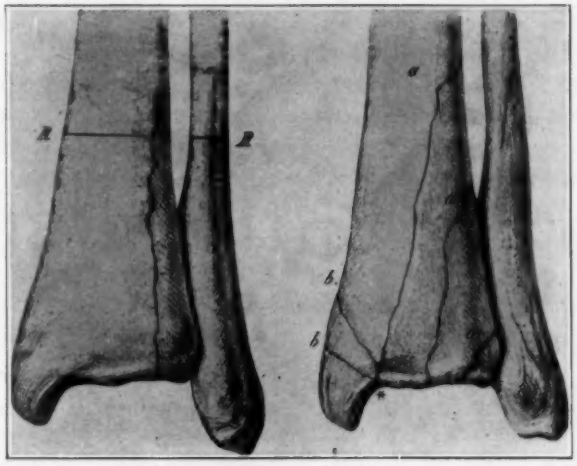

Fig. 5.—Left, von Volkmann's illustration of the case in which at operation he found (1) fracture of the medial malleolus, (2) fracture of the fibula and (3) fracture of the tibia anterolaterally with a fragment torn off corresponding to the insertion of the ligamentum malleoli lateralis anterius, the membrana interossea and the anterior part of the ligamentum interosseum tibiofibulare. The fracture line has a sagittal course. Von Volkmann reported that in this type of fracture the ligaments of the syndesmosis are most frequently detached from the tibia without so large a fragment. Right, von Volkmann's illustration of his hypothetic explanation of the occurrence of anterior and lateral fractures of the tibia and of the medial malleolus.

fibula or interosseously between the two fragments of the tibia. The talus may luxate upward either between the two fragments of the tibia or between the tibia and fibula, according to which lesion has been sustained. Fracture of the medial malleolus finally occurs.

In an illustration by von Volkmann (fig. 5, right) it is seen that he believed the lateral fragment of the tibia may be small or large, and that in the extreme case it may occupy the whole of the anterior articular surface of the tibia, so that its fracture line distally stretches

to the fracture line in the medial malleolus. To this must be added that I have never seen, on roentgenograms from the daily work in the roentgen department or in literary works on fractures of the ankle, fractures of the tibia of this nature in connection with fibular fracture above the lateral malleolus, and of the medial malleolus.

It is seen that the order in which von Volkmann stated the lesions to occur is different from that indicated in abduction fractures in Dupuytren's [13] theory and from that shown by the experiments of Bonnet [20] and Huguier.[25] Later in this work it will be shown that von Volkmann's conception about the mechanism must be considered to be incorrect.

With regard to another form of fracture which von Volkmann mentioned, he said that a large anterior bony wedge was torn from the anterior distal part of the tibia, that the talus was luxated forward and the line of fracture was exactly in the frontal plane. Von Volkmann did not say anything about the mechanism of this fracture. According to the description it must be a case of the type of fracture which nowadays is designated as a large fragment torn from the anterior lip of the tibia in connection with forward subluxation of the talus, and which is produced when a fall causes the foot to be dorsiflexed beyond the physiologic limit.

It is obvious from von Volkmann's description and diagram that the so-called "Volkmann triangle" is found anterolaterally or frontally, and not laterally, as has been maintained by Svend Hansen,[28] or dorsally, as practically all German authors have stated, who by so doing erroneously have classified it as what is now commonly described as fracture in the dorsal lip of the tibia.

A detailed account of von Volkmann's own statements is given here, as these assertions must be due to misconceptions of von Volkmann's literary works and as up to the present day highly different views have been set forth concerning that which von Volkmann found and described in his operative cases, both in discussions and in the literature. It must be emphasized that von Volkmann in two widely different forms of fractures of the ankle saw fragments torn away from the tibia, either anterolaterally or frontally, and that he plainly pointed out that in the

28. Experimentally Svend Hansen [24] produced fracture by chiseling off the whole of the lateral margin of the tibia, so that a conical fragment was produced, the base of which was slightly more than 2 cm., and the height and width of which were 3 cm. Svend Hansen made roentgenograms of this fracture, which could be seen on the frontal picture. I have never seen a roentgenogram of this form of fracture, although I have examined films from many hundred patients with fractures of the ankle and have studied reproductions of roentgenograms in approximately three hundred and fifty literary works on fractures of the ankle. Svend Hansen himself stated in his thesis (page 45) that no fracture of this kind was found in his material. The anatomic conditions (the ligaments) at the distal part of the lateral surface of the tibia are such that neither do they seem to cause a lateral tibia fracture. The clinical occurrence is surely very doubtful.

form of fracture in which a fragment was produced anterolaterally by tearing of ligaments, this was rarely—exceptionally—of such a dimension as he found it at operation, and as his diagram showed.

The type of fracture which Pott [8] was the first to describe and illustrate, which Cooper [18] and Malgaigne [21] later on found by inward luxation of the tibia, which Huguier [25] produced experimentally and which, von Volkmann [27] found at operation (in the first case cited in a foregoing paragraph), must according to the descriptions of the pathologico-anatomic picture given by the various writers be supposed to be the same type of fracture.

Huguier reported that the fracture is produced by external rotation of the foot, while the clinical authors recorded that it occurs by abduction and pronation.

J. O. Hönigschmied [29] (1877) made experiments with fractures, inspired to do so by Bonnet.[20] He produced fractures of the ankle by forced movements of the foot, and his observations were as follows:

By adduction fracture of the lateral malleolus or rupture of the lateral ligament was produced. The fracture of the fibula did not occur proximal to the level of the distal articular surface of the tibia, and as a rule its seat was 1 cm. above the tip of the lateral malleolus. In case of rupture of the lateral ligaments these were torn from the tip of the malleolus with a bony shell.

By abduction a variety of lesions occurred. He fixed the foot below both malleoli in a vise, and the abduction was brought about by moving the crus laterally.

In some cases the deltoid ligament was torn from the medial malleolus. In other cases a fracture of the medial malleolus occurred on a level with the articular surface of the tibia. Sometimes a lesion of the ligaments between the talus-calcaneus and os naviculare was produced.

Like Bonnet, Hönigschmied thus produced by abduction primary fracture or rupture of ligaments at the medial malleolus, but no secondary fibular fracture, and like Maisonneuve and Bonnet he produced primary lesion in the lateral malleolus distal to the talocrural joint by adduction.

By external rotation of the foot Hönigschmied also produced a variety of lesions in the ankle region.

In little more than one half of the experiments a spiral fracture occurred in the distal end of the fibula with the course of the fracture line like that stated by Maisonneuve. Hönigschmied reported that in a great number of the cases the fracture was found on a level with the distal articular surface of the tibia.

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29. Hönigschmied, J.: Leichenexperimente über die Zerreissungen der Bänder im Sprunggelenk mit Rücksicht auf die Entstehung der indirekten Knöchelfracturen, Deutsche Ztschr. f. Chir. **8**:239, 1877.

In the rest of the cases there was detachment of the ligamentum malleoli lateralis anterius with a small bony shell torn away from the tibia, and in most cases also rupture of the ligamentum interosseum tibiofibulare. He reported that in that group the fibular fracture was found in some cases from 4.5 to 7 cm. above the tip of the malleolus, and in some cases in the upper third of the bone. In these cases there were thus ascertained "diastasis" and also rupture of the deltoid ligament at the medial malleolus.

Thus Hönigschmied, by forced external rotation of the foot, observed oblique spiral fracture distally in the fibula in some cases, fracture of this bone 4.5 cm. or more above the tip of the lateral malleolus in some cases and in the proximal end of the fibula in some cases.

It should be noted that there is this difference between the results of the experiments by Maisonneuve [14] and Hönigschmied, that the latter in the cases in which diastasis occurred found the fibular fracture sometimes at the proximal end and sometimes from 4.5 to 7 cm. above the tip of the lateral malleolus, while in the case of diastasis Maisonneuve always found a high fibular fracture.

On the other hand, Hönigschmied and Huguier [25] agree as far as the fibular fracture is concerned when it occurs in association with diastasis (the fibular fracture is always more than 3½ inches [8.9 cm.] above the tip of the malleolus and sometimes in the proximal end of the fibula).

Hönigschmied stated that by external rotation of the foot it passes into pronation position, but did not say that he actively kept it pronated during the external rotation. He agreed with Maisonneuve that the oblique spiral fracture distally in the fibula is the most common fracture in this bone.

Verneuil (1882) published in *Bulletins et mémoires de la Société de chirurgiens de Paris* several cases of clinical fractures of the anterolateral corner in association with sprain of the syndesmotic ligaments frontally, and the term *fragment intermediaire* is applied to this form of fracture.

Leon le Fort [30] (1886) observed and described 3 clinical cases of isolated fracture of the anterior margin of the lateral malleolus corresponding to the attachment of the ligamentum malleoli lateralis anterius. In his opinion the fracture is produced by forced supination-adduction of the foot.

L. le Roy [31] (1887), who was a pupil of le Fort, made experiments on cadavers with a view to ascertaining the mechanism of this fracture. Like le Fort he arrived at the result that the fracture is produced by

30. Le Fort, L.: Note sur une variété non décrete de fracture verticale de la malléole externe par arrachement, Bull. gén. de thérap. **110**:193, 1886.

31. Le Roy, L.: De la fracture marginale antérieure de la malléole externe, Paris, 1887.

adduction and supination of the foot. More particularly he pointed out how his experiment (no. 24) seemed to illustrate this. He reported that in this experiment by forced supination and adduction of the foot a fracture was produced, the surface of which had a vertical course and the distal fragment of which consisted of the portion of the bone to which the ligamentum malleoli lateralis anterius, the ligamentum talofibulare anterius and the ligamentum calcaneofibulare are attached.

The isolated fracture in the lateral malleolus found by le Roy in experiment 24 had, however, not the localization which le Fort recorded for his fracture, which was expressly stated to be confined to the attachment of the ligamentum malleoli lateralis anterius at the proximal corner of the anterior margin of the lateral malleolus.

In other experiments le Roy applied forced external rotation of the foot in order to see what happened, and he observed that in 9 cases the ligamentum malleoli lateralis anterius was torn off with a bony shell; six times the detachment was from the tibia and three times from the lateral malleolus.

In spite of the fact that the results of these experiments rather suggested that by external rotation of the foot he produced the fracture ascertained by le Fort, he emphasized that it was produced by supination and adduction. His interpretation of the results is surely incorrect. The result of experiment 24 shows it directly, as the fracture he produced was an adduction fracture with primary fracture involving avulsion of the apical part of the lateral malleolus and secondary fracture of the medial malleolus. His experiments were thoroughly carried out and reported; the misinterpretation may be due to the fact that le Fort, his preceptor, had so vigorously emphasized that the fracture of the lateral malleolus was produced by supination-adduction, or to the fact that the avulsion of the ligament by external rotation of the foot oftener occurred from the tibia than from the malleolus.

Thus le Roy's experiments seemed to show that by external rotation of the foot avulsion of the ligamentum malleoli lateralis anterius is produced with small fragments from the tibia or lateral malleolus. The results of his experiments thus corroborated, though he did not realize it himself, the correctness of both Verneuil's and le Fort's clinical observations concerning isolated fracture in the anterolateral corner of the tibia and in the anterior margin of the lateral malleolus.

Tillaux [32] (1890) stated concerning the movements of the foot that in addition to plantar flexion and dorsiflexion a slight rotation is possible in the talocrural joint.

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32. Tillaux, P.: Traité de chirurgie clinique, Paris, Asselin & Houzeau, 1889, vol. 2, p. 842; Traité d'anatomie topographique, ed. 6, Paris, P. Asselin, 1890, p. 1075.

The latter movement takes place around a vertical axis by a slight rotation of the talus around the medial malleolus as the fulcrum. He added that in order that this movement, by which the foot is moved inward and outward, will be possible, there must at the same time be a certain plantar flexion and dorsiflexion of the foot respectively, as the talus can only rotate in this manner because of its smaller width in the posterior part, which by dorsiflexion will be in the malleolar fork.

Adduction and abduction take place in the articulation of the talus with the calcaneus and the os naviculare. By extreme degrees of these movements the malleolar fork is affected, and if they are continued beyond a certain limit a malleolar lesion is produced. In conformity with this description of the rotation of the talus in the talocrural joint Tillaux, like Malgaigne,[21] believed that the adduction and abduction movements are combined with internal and external rotation of the foot respectively. Tillaux maintained that it is this which caused Maisonneuve [14] to believe that the external rotation as such may cause a fracture of the fibula. It is seen that both Tillaux and Malgaigne thought that because of the articular construction of the foot and the talocrural joint the anterior part of the foot is everted by abduction. Tillaux tried to explain the reasons for this disagreement with Maisonneuve.

Tillaux' experimental-surgical investigations aimed at refuting Maisonneuve's statements. First he carried out experiments by way of a forced adduction movement, by which avulsion of ligaments at or fracture in the distal half of the lateral malleolus were obtained. This fracture was often transverse and followed by a secondary lesion in the medial malleolus, so that in this experiment he arrived at the same result as Bonnet.[20] Instead of the fracture in the medial malleolus a fracture of the tibia sometimes occurred just above the articular surface.

By forced abduction movement (the foot is pronated at the same time), Tillaux stated, the dorsum of the foot is turned inward and the planta outward and the anterior part of the foot is directed outward.

As the primary lesion he produced rupture of the deltoid ligament or fracture of the medial malleolus—roughly transverse. The secondary lesion was avulsion of the ligaments distally between the tibia and fibula with a small osseous fragment from the tibia (*fragment troisième*) accompanied by some diastasis. If the lesion was continued, a fracture of the fibula occurred 5 to 6 cm. above the tip of the lateral malleolus.

With regard to the bone torn from the tibia Tillaux himself did not say anything about its seat, whether anterolateral or dorsolateral.

Thaon [33] (1870) reported an autopsy in which he found a large fragment torn away from the posterior lip of the tibia. At the same

33. Thaon: Fracture du péroné: Phlegmon gangréneux alcoolique, Bull. Soc. anat. de Paris (1870) **45**:212, 1874.

time he stated that he had often seen fragments from the posterior lip in the experiments carried out by Tillaux.

Souligoux [34] (a pupil of Tillaux) published in 1912 two diagrams by Tillaux which had not been published before. Anteriorly they showed a small fragment corresponding to avulsion of the tuberculum anterius tibiae, while posteriorly a somewhat larger fragment corresponding to the tuberculum posterius tibiae was seen. According to this it must be presumed that Tillaux had been of the opinion that fragments from both the tuberculum anterius tibiae and the tuberculum posterius tibiae might represent *fragment troisième.*

By his experiment Tillaux did not find proof of the incorrectness of Maisonneuve's theory, but in details and on the whole proof of the correctness of Dupuytren's theory about the production of fractures by abduction. His observation that abduction of the foot in pronated position necessarily involves external rotation of the anterior part of the foot is also correct, but does not prove that forced external rotation of the foot cannot produce the fibular fracture which Maisonneuve presented in his experiments. By my own experiments and clinical material I will prove in a subsequent paper that the fractures produced by Tillaux and Maisonneuve must be presumed to be brought about by two widely different mechanisms of fracture.

Dunand,[35] who also made experimental-surgical investigations, could not produce diastasis by abduction and external rotation of the foot. If, however, he previously cut the deltoid ligament or fractured the medial malleolus, he always succeeded in producing diastasis by external rotation of the pronated-abducted foot.

Lewis A. Stimson [36] (1892) stated that in Pott's fracture there are rupture of the ligament at or fracture of the medial malleolus, rupture of the ligamentum malleoli lateralis anterius with a small fragment torn from the tibial attachment and a fracture of the fibula up to 3 inches above the tip of the malleolus. He assumed that this fracture occurs by abduction and external rotation of the foot.

His conception is stated here in order to give prominence to his explanation of the genesis of one of these lesions, rupture of the ligamentum malleoli lateralis anterius.

He performed experimental-surgical investigations and observed that when there is forced external rotation of the foot the primary lesion is rupture of the ligamentum malleoli lateralis, as a small bony shell is torn from its tibial attachment, and the secondary is an oblique spiral fracture in the distal end of the fibula just proximal to the talocrural

34. Souligoux: A propos du fragment marginal postérieur dans les luxations du pied en arriere, Bull. et mém. Soc. de chir. de Paris **38**:1103, 1912.

35. Dunand, M.: De la diastasis traumatique simple de l'articulation péronéo-tibiale inférieure, Paris, 1878.

36. Stimson, L. A.: Pott's Fracture at the Ankle, New York M. J. **55**:701, 1892.

joint. Stimson himself maintained that Pott's fracture is produced by abduction of the foot and that the fracture of the medial malleolus is the primary injury and cited his experiment as a proof that by abduction of the foot, the anterior part of which during this movement is rotated externally, a rupture of the ligamentum malleoli lateralis anterius takes place in connection with fracture of the medial malleolus and the fibula. He did not realize that the detachment of the ligament which he produced primarily in his experiment must be caused by a mechanism of fracture which is quite different from that which, according to his statement, should produce Pott's fracture.

Even though it is possible to show the inconsequence of his argument, Stimson's observation that rupture of the ligamentum malleoli lateralis anterius is produced by external rotation of the foot and that it appears before the oblique spiral fracture in the distal end of the fibula is nevertheless of importance.

Maisonneuve [14] was the first to produce the oblique spiral fracture in the distal end of the fibula by forced external rotation of the foot.

Stimson was the first who experimentally showed that rupture of the ligamentum malleoli lateralis anterius takes place before the oblique spiral fracture in the distal end of the fibula occurs.

Yet Stimson was not aware of the connection between these two lesions, which appears from the fact that he did not associate the rupture of the ligament with Maisonneuve's oblique spiral fracture in the fibula, but (wrongly) thought that it is only a feature of the Pott fracture.

Souligoux [37] (1896) demonstrated by means of a specimen how he thought that fracture of the medial malleolus, diastasis, and fibular fracture 5 to 6 cm. above the tip of the malleolus occur.

By abduction and external rotation of the foot the primary lesion is fracture of the medial malleolus; then the talus adopts a valgus position and, if the movement is continued, the lateral malleolus is affected, so that rupture of the ligament and diastasis and finally fracture of the fibula occur.

E. Quénu [22] (1907) carefully reviewed existing literature on fractures of the ankle in order to ascertain whether there were any statements which might suggest that diastasis had been noted at operation, autopsy or in fractures produced experimentally and, in such case, in which types of fracture diastasis had been found and by what mechanisms of fracture it had been produced.

It is not evident from Quénu's work whether he knew of Stimson's [36] experiments or the experimental-surgical investigations published by le Roy [31] in 1887.

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37. Souligoux: Du mécanisme des fractures des malléoles, Assoc. franç. de chir., Proc.-verb. **10**:724, 1896.

By experiments on cadavers he observed that by external rotation of the foot in supinated position the ligamentum malleoli lateralis anterius is tightened and that by increased application of force this ligament is torn off with a bony shell from the anterior surface of the tibia, and then diastasis between the tibia and fibula occurs, so that the intermalleolar distance is increased by 1 cm. If the rotating force ceases at that point, the fibula again adopts its normal position in relation to the tibia. If, on the other hand, the external rotation is further increased after the ligamentous rupture, an oblique spiral fracture occurs distally in the fibula.

Quénu came to the conclusion that no one had previously attempted to produce fractures of the ankle by external rotation of the supinated foot.

Quénu was the first who by experiments primarily produced rupture of the ligamentum malleoli lateralis anterius and secondarily oblique spiral fracture in the distal end of the fibula by external rotation of the supinated foot.

From the reports cited it appears that at the beginning of the twentieth century considerable results were at hand which had been achieved by researches in the field of fractures of the ankle during the nineteenth century, but that vagueness and consequently a considerable divergence of views still prevailed as to the mode or modes of production, the pathologic anatomy and the clinical diagnosis of fractures of the ankle. Research workers who carried out experimental surgery and elaborately studied fractures of the ankle appear almost invariably to have worked rather one-sidedly with a few individual forms of fractures of the ankle and most frequently to have advanced clinical observations and experimental achievements as proofs against the results attained by contemporary or former researchers instead of regarding them as what they really were, discoveries of so far unobserved features of the problem.

In the interval between Dupuytren [18] and the twentieth century no one tried to disentangle the real facts of fractures of the ankle by a close comparison of the multifarious results of researches achieved during the nineteenth century by way of experimental surgery and clinical and pathologicoanatomic studies.

As the introduction of roentgen diagnosis means the beginning of a new epoch of the research of fractures, it will be appropriate, before I begin a review of the roentgenographic period, to summarize the stage of research at the beginning of this period.

*Fractures Due to Forced Adduction.*—According to Dupuytren's theory fractures should occur primarily in the lateral malleolus and secondarily in the medial malleolus by this movement.

By outward luxation of the tibia adduction fractures were observed by Cooper [18] and Malgaigne.[21] Clinically they were observed by M. T.

Boyer [19] and Malgaigne as bimalleolar fractures and *fractures bimalleolaires par adduction* respectively.

Experimentally they were uniformly produced by Dupuytren,[13] Maisonneuve,[14] Bonnet,[20] Hönigschmied,[29] Tillaux [32] and le Roy [31] with the primary lesion in the distal half of the lateral malleolus. Bonnet [20] and Tillaux [32] produced both the primary and secondary lesions of the bone by adduction fracture in their experiments.

*Fractures Due to Forced Abduction of the Pronated Foot.*—Dupuytren's [13] theories suggest that abduction fractures should occur primarily in the medial malleolus and secondarily in the lateral malleolus.

In conformity with this the first stage was experimentally produced by Bonnet [20] and Hönigschmied.[29]

In its entirety the fracture was produced by Tillaux [32] by abduction of the pronated foot, by which the primary lesion was a roughly transverse fracture of the medial malleolus at the base, the secondary was ligamentous rupture between the tibia and fibula with avulsion of a bony shell from the tibia laterally *(fragment troisième)*, and thirdly a fracture of the fibula just proximal to the malleolus was produced.

Clinically it was observed by M. T. Boyer as bimalleolar fracture.

*Fractures Due to External Rotation of the Foot.*—By external rotation (or, according to the clinicians' statements, abduction and pronation of the foot) fractures of two widely different types were produced.

1. (*a*) Detachment of the ligamentum malleoli lateralis anterius with a bony shell torn from the anterior lip of the tibia or the anterior margin of the lateral malleolus.

   (*b*) Oblique spiral fracture in the distal end of the fibula.

Maisonneuve [14] was the first who experimentally produced the oblique spiral fracture in the distal end of the fibula by external rotation of the foot. Hönigschmied [29] did the same later on. Le Roy [31] produced detachment of the ligamentum malleoli lateralis anterius with a bony shell torn from either the tibial or the malleolar attachment by external rotation of the foot.

Stimson [30] produced in his experiments primarily detachment of the ligamentum malleoli lateralis anterius and secondarily the oblique spiral fracture in the distal end of the fibula by external rotation.

Quénu [22] obtained the same result as Stimson by external rotation of the supinated foot.

Clinically Verneuil observed isolated fracture of the anterior margin of the malleolus, and le Fort [30] isolated fracture of the tibia anterolaterally.

By total and partial forward luxation of the tibia Cooper [18] found at autopsy these two lesions plus, in 2 cases of this nature, a dorsal fracture of the distal articular surface of the tibia.

At operation R. Adams [38] observed cases of this last type. Richard [39] reported cases similar to those cited by Adams.

2. (*a*) Ligamentous rupture at or fracture of the medial malleolus.

(*b*) Ligamentous rupture with avulsion of bony shell in the syndesmotic connection between the tibia and the fibula distally, so that diastasis occurred; the ligamentous ruptures were of greater extent than those mentioned under group *a*

(*c*) Fracture of the fibula 4.5 cm. or more above the lateral malleolus.

Maisonneuve [14] produced by external rotation of the foot ligamentous rupture and diastasis distally between the tibia and the fibula and then fracture in the proximal end of this bone.

Huguier [25] produced ligamentous rupture at the medial malleolus, in the distal tibiofibular articulation and fibular fracture 4.5 cm. or more above the lateral malleolus (in 2 cases in the proximal end of the fibula). Hönigschmied [29] found by his experiments partly what Maisonneuve and partly what Huguier had ascertained by external rotation of the foot.

Dunand,[35] after having cut the deltoid ligament, produced by external rotation of the pronated foot ligamentous rupture between the tibia and the fibula distally and diastasis, and then fibular fracture some centimeters above the lateral malleolus.

Cooper [18] and Malgaigne [21] by inward luxation of the tibia observed rupture of the ligament at or fracture of the medial malleolus, rupture of the ligament distally between the tibia and fibula with avulsion of a bony shell from the tibia anterolaterally and fracture of the fibula 3½ inches above the tip of the lateral malleolus.

R. von Volkmann [27] at operation made a similar observation (the line of fracture in this case was approximately in the sagittal plane [fig. 5 left]). The fracture was observed clinically and described by Dupuytren [13] as abduction fracture and by Malgaigne [21] as *fracture bimalleolaire par abduction* or as supramalleolar fracture.

This fracture, produced experimentally—with some variation—by various researchers and found at operations and autopsies by clinicians, corresponds in all essentials to the type of fracture described by Pott.

The fact that the experimenters by forced external rotation produced two so widely different types of fracture as have been listed here under 1 and 2 might suggest that factors other than the external rotation of the foot played a decisive part in the production of the fractures and that these factors in connection with the external rotation might condition the production of the two types of fractures. The

38. Adams, R., in Todd, R. B.: The Cyclopaedia of Anatomy and Physiology, London, Longman [and others], 1836, vol. 1, pp. 154-161.

39. Richard, A. M., in Duplay, S.: Traité de chirurgie, Paris, G. Masson, 1890, vol. 1, p. 1; Pratique journalière de la chirurgie, Paris, Germer-Baillière, 1868, p. 71.

fact that the clinicians stubbornly maintained that fractures of this kind were not produced by external rotation, but by abduction, and the result of Dunand's experiment seem to indicate that the combination of external rotation and abduction is decisive for the production of the fractures in group 2.

After I have presented the results of my own experiments this point will be discussed in detail.

On the introduction of roentgenographic diagnosis the research on fractures involving the ankle by experimental surgery and by autopsy came to a complete standstill, as at that time the roentgen method fairly soon became popular among the clinicians, who thought that they did not need to depend on the experimental-surgical results achieved by previous researchers with regard to the genesis and classification of fractures of the ankle, as it appeared that roentgen examination provided an easy, quick and far surer method of ascertaining the presence and number of fractures, dislocation and accompanying luxation, if any.

Respecting the mechanics of the production of fractures one should consult Jean-Louis Petit,[4] Malgaigne,[21] Gosselin,[40] Gerdy,[41] Larrey,[42] W. Koch,[43] Kroell [44] and H. Zuppinger.[45]

### THE ROENTGENOGRAPHIC PERIOD

By means of roentgenographic diagnosis clinicians now found not only such fractures as had previously been known but also marginal fractures of the tibia, and among the latter most frequently fracture of the dorsal lip of the tibia, and diastasis between the tibia and fibula to an extent which had not previously been imagined.

In the following years these two components became the main subjects of the research on fractures of the ankle in order to throw light on their diagnosis, frequency and importance for the prognosis, and their importance as a complication of malleolar fractures at the planning of treatment.

Furthermore, the classification of fractures of the ankle gave rise to many reflections.

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40. Gosselin, L.: Clinique chirurgicale de l'hôpital de la Charité, ed. 3, Paris, J.-B. Baillière et fils, 1879, lessons 40-42.

41. Gerdy, P.-N.: Maladies des organes du mouvement, os, muscles, etc., en général, Paris, V. Masson, 1855.

42. Larrey: Traitement des fractures, Compt. rend. Acad. d. sc. **5**:650, 1837; Rapports sur une nouvelle méthode de traiter les fractures, ibid. **5**:676, 1837.

43. Koch, W.: Ueber Torsions-fracturen, Berl. klin. Wchnschr. **2**:140, 1874.

44. Kroell, O.: Ueber Spiralfracturen, Leipzig, J. B. Hirschfeld, 1888; Deutsche Ztschr. f. Chir. **28**:1, 1888.

45. Zuppinger, H., cited by Ramsperger.[120]

It will be natural to treat the subject under the following headings:

1. Marginal fractures of the tibia:
   (*a*) Fractures involving the posterior lip of the tibia.
   (*b*) Fractures involving the anterior lip of the tibia.
2. Rupture of the syndesmosis—diastasis.
3. Classification of fractures of the ankle.
4. Reduction and retention of fractures of the ankle.

1. *Marginal Fractures of the Tibia.*—(*a*) Fractures Involving the Posterior Lip of the Tibia: As already mentioned, several earlier researchers (Cooper,[18] Earle,[46] Adams,[38] Dupuytren,[13] Malgaigne,[21] Nélaton,[47] Thaon,[28] Gurlt [48] and Richard [39]) had in autopsy specimens and at operations ascertained that in association with malleolar fracture there might be a fracture in the distal articular surface of the tibia dorsally, a form of fracture which in older times had been considered rare. Only Rochet [49] has tried experimentally to produce this fracture by dropping a weight of 60 Kg. on the upper end of the tibia while the foot was plantarflexed.

Chaput [50] (1899) was the first to demonstrate a roentgenogram of a fracture in the dorsal lip of the tibia, and already at that time he suggested that it was frequently observed as a complication of malleolar fractures; subsequently he observed it forty-two times in 136 fractures of the ankle.

After that Destot [23] dealt thoroughly with the problem of fracture in the dorsal part of the tibia; like Chaput, he found that this fracture was common; he discovered it one hundred and forty-five times in 1,700 fractures of the ankle. Initially he thought that the fracture in the dorsal lip of the tibia was an entirety in connection with another fracture in the ankle region, but later on—when he himself and others believed to have found cases of isolated fracture of the posterior lip of the tibia—he alleged that the fracture must be the first lesion caused by a mechanism of fracture which also produced the malleolar fractures with which it was combined.

Destot continued his studies both of this fracture and of all the other marginal fractures of the tibia, and after the discussion in *Bulletins et mémoires de la Société de chirurgiens de Paris* in November

46. Earle: Simple, Succeeded by Compound Dislocation Forward of the Inferior Extremity of the Tibia, Lancet **2**:346, 1828-1829.

47. Nélaton, A.: Elémens de pathologie chirurgicale, ed. 2, Paris, Germer-Baillière, 1874, vol. 3, p. 296.

48. Gurlt, E.: Handbuch der Lehre von den Knochenbrüchen, Hamm, 1862-1864.

49. Rochet, V.: Du mécanisme des luxations doubles de l'astragale (énucléation), Rev. d'orthop. **1**:269, 1890; cited by Ashhurst.[60]

50. Chaput, V.: Les fractures malléolaires du cou-de-pieds et les accidents du travail, Paris, Masson & Cie, 1907; De la réduction des fractures malléolaires compliquées de luxation du pied, Bull. et mém. Soc. de chir. de Paris **38**:656, 1913.

1906 he summarized the position, that there might be the following marginal fractures of the tibia: 1. A small fragment might be torn off from the tibia anterolaterally. 2. The *fragment troisième* experimentally produced and found by Tillaux was an independent injury. 3. The rather large fragment which was produced by the actual fracture in the dorsal part of the tibia was quite different from *fragment troisième,* since its considerable size and its form made it unlikely that it had been produced by avulsion. In Destot's opinion it was chipped off by maximal plantar flexion and backward displacement of the talus, in conformity with what the earlier writers (Cooper,[18] Earle,[46] Adams,[38] Dupuytren,[13] Gurlt,[48] Richard,[39] Malgaigne [21] and Lucas-Championnière [51]) had previously maintained. Destot believed that this fracture must be supposed to have been present in all the cases which earlier writers had mentioned as dorsal luxation of the foot.

Pels Leusden [52] (1905) also frequently found fracture in the posterior lip of the tibia in connection with malleolar fracture; he saw that these fractures were often associated with dorsal luxation of the foot and introduced the descriptive term luxation fractures. In his opinion they ought, if the term were absolutely correct, to be called fracture luxations, since luxation of the foot was found only in connection with fractures which were the primary injury, while the luxation was a complication. Pels Leusden examined roentgenograms of 6,000 lesions of the ankle and found among them not 1 case of luxation without fracture, and thus ascertained that luxation in the talocrural joint is found only in connection with fracture.

Grashey [53] (1907), too, found often fracture in the posterior lip of the tibia in connection with dorsal luxation of the foot and malleolar fracture. He could not imagine how these fractures were produced by the same mechanism. He never found isolated fracture in the posterior lip of the tibia.

Meissner [54] (1909) pursued the study of fractures of the ankle because, like the other authors mentioned, he often by roentgen examinations found fracture in the dorsal part of the tibia together with fractures of the ankle and because he attached great importance to this fracture for the backward displacement of the foot. He found it in 19 cases out of 160 fractures of the ankle.

Eugen Bircher [55] (1912) wrote that the fracture in the posterior lip of the tibia might sometimes exist, but in such a way that it was not

51. Lucas-Championnière, J.: Deformation des fractures vues et éxagerées par la radiographie, J. de méd. et chir. prat. **71**:49, 1900.

52. Pels Leusden, F.: Ueber Verrenkungen und Verrenkungsbrüche in Talocruralgelenk, Berl. klin. Wchnschr. **42**:109 and 152, 1905.

53. Grashey, R.: Ueber die Untersuchung von Frakturen mit Röntgenstrahlen, Fortschr. a. d. Geb. d. Röntgenstrahlen **11**:139, 1907.

possible to find it on the roentgenogram immediately after the accident, while with a subsequent roentgen examination a shell-shaped strip of callus was found. He saw 2 cases of this kind and 5 cases in which it was possible to observe an actual fracture in the posterior lip of the tibia. From this he concluded that the fracture in the dorsal lip of the tibia must be supposed to be produced by ligament tearing and that in the 2 cases first mentioned, in which there was a so-called fractureless formation of callus, there were lesions which were analogous with fractures in the posterior lip of the tibia.

Demoulin[56] (1913) reported that there were two categories of fractures in the posterior lip of the tibia, small and large fragments.

N. Backer Grøndahl[57] (1913) classified the fractures involving the dorsal distal part of the tibia into three groups: (1) fracture in the dorsal tibial lip proper; (2) fractures in the posterolateral corner of the tibia, and (3) fractures consisting of cortical avulsion from the dorsal surface of the tibia. He indicated that the first group of fractures was intra-articular, which was not the case with the two later groups.

Souligoux[58] (1913) described the pathologicoanatomic condition of fracture dorsally in the tibia and reported that in some cases only the tuberculum posterius was fractured, but the rest of the posterior lip of the tibia was intact, while in other cases the entire lower posterior lip of the tibia was torn off, either as a thin bony lamella or as a conic fragment, on the wider base of which there was a piece of the tibial articular surface of varying size. Tanton[1] (1916), too, made a thorough study of the fracture of the posterior lip of the tibia.

Cotton[59] (1915) described fracture in the posterior lip of the tibia as a new type of fracture of the ankle, which, as may be understood, aroused a certain amount of surprise. This publication was, however, as Ashhurst put it, of good use, as it stimulated the interest in this particular fracture. At that time the fracture was so unknown in America that as a result of the publication it was often afterward called "Cotton's fracture."

Svend Hansen[24] (1919) found fracture in the dorsal lip of the tibia fifty-nine times out of 153 fractures of the ankle; i.e., that this

54. Meissner: Beiträge zur Kenntniss der Malleolenfrakturen, Beitr. z. klin. Chir. **62**:78, 1909; Eine typische Fraktur der Tibia in Talo-cruralgelenk, ibid. **61**:136, 1908.

55. Bircher, E.: Abrissfraktur am Malleolus lateralis tibiae posterior, Zentralbl. f. Chir. **39**:171, 1912.

56. Demoulin: Luxation récidivante de la mâchoire inférieure, Bull. et mém. Soc. de chir. de Paris **39**:1030, 1913.

57. Grøndahl, N. B.: Fractura marginalis posterior tibiae og andre bruddkomplikationer ved ankelbrudd, Norsk. mag. f. lægevidensk. **11**:737, 1913.

58. Souligoux: Des fractures du cou-de-pied, Tribune med. **47**:1, 1913.

59. Cotton, F. J.: A New Type of Ankle Fracture, J.A.M.A. **64**:318 (Jan. 23) 1915.

fracture was found in more than one third of all such cases. He reported 1 case in which a fracture involving the posterior lip of the tibia was observed at autopsy in connection with fracture of the medial malleolus, oblique spiral fracture in the distal end of the fibula and a small fragment torn from the anterolateral corner of the tibia (detachment of the ligamentum malleoli lateralis anterius). The proximal fibular fragment was in normal ligamentous connection with the tibia and the lateral malleolar fragment in normal connection with the foot and the fragment from the dorsal lip of the tibia by intact ligaments. The base of the fragment torn from the dorsal lip of the tibia was 1.5 cm. wide and represented about one third of the cartilage-covered articular surface. The fragment was of equal medial and lateral width; its form viewed from the side was like a cone, and its height was roughly 2.5 cm.

With regard to the roentgen examination and the establishment of the fracture in the dorsal distal part of the tibia he arrived at the result that when on the lateral roentgenogram it was possible to diagnose fracture in the dorsal distal part of the tibia, the fracture involved not only the tuberculum posterius but also the dorsal lip of the tibia.

Ashhurst [60] (1922) reported a similar ratio of incidence of fracture in the posterior lip of the tibia. He declared as his personal opinion that, after having compared the views of the various authors, it is impossible to make a distinction between a fragment consisting of the posterior lip of the tibia proper and a fragment involving the tuberculum posterius tibiae alone.

E. Husfeldt [61] (1938) reported that by roentgenograms taken in an oblique side projection extra-articular fracture in the tuberculum posterius tibiae might be distinguished from fracture in the posterior lip of the tibia proper, which, however, must be supposed to be incorrect.

As far as the isolated fragment of the dorsal lip of the tibia is concerned, several cases were published subsequent to Meissner;[54] e.g., by Quénu,[22] Routier,[62] Hilgenreiner [63] and Destot.[23] Poul Billet [64] compiled these cases and maintained in his thesis that the existence of the isolated fracture of the tibial lip must be considered a fact. Svend Hansen,[24] Thore Walheim [65] and S. Franck [66] reported additional cases.

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60. Ashhurst, A. P. C.: Double Fracture of the Tibia Involving the Ankle Joint, Ann. Surg. **75**:243, 1922.

61. Husfeldt, E.: Treatment of Malleolar Fractures, Hospitalstid. **81**:717, 1938.

62. Routier: Fracture marginale postérieure isolée, Bull. et mém. Soc. de chir. de Paris **38**:1503, 1912.

63. Hilgenreiner, H.: Die Extensions- und Flexionsfraktur am unteren Ende der Tibia und Fibula, Beitr. z. klin. Chir. **87**:384, 1913.

64. Billet, P.: Fracture isolée de la malléole postérieure, Thesis, Lyon, no. 73, 1913.

Tanton [1] believed also that he had found isolated fracture in the dorsal lip of the tibia, but stated that it seemed to appear in two forms: (1) *fracture isolée pure (en torse)* (purely isolated fracture [sprain] and (2) *fracture margino-tibio-malleolaire* (marginal fracture of the tibia combined with fracture of the medial malleolus). A characteristic feature of both was that there was no dislocation of the foot.

Grashey [53] and Husfeldt [61] found no cases of isolated fracture in the dorsal lip of the tibia in their material.

By a closer study of Meissner's [54] article concerning the first case published it will be seen that it was actually not a case of isolated fracture involving the dorsal lip of the tibia, as Meissner distinctly stated that it was certain that as a complication rupture of the deltoid ligament with avulsion of bone from the medial malleolus could be ascertained.

With regard to the other cases referred to it may be ascertained by going through the case records that there are symptoms which may indicate that in these cases also the isolated fracture in the dorsal lip of the tibia was not the only lesion. As to Routier's case, it was reported that "articular diastasis" was found, and in several of the other cases there were tenderness and ecchymosis around the medial malleolus or on the anterior surface of crus corresponding to the syndesmosis, which must be interpreted as a symptom of a concurrent lesion here.

Svend Hansen [24] stated that there were 2 cases of isolated fracture in the tibial lip in his material. By examination of the roentgenograms which demonstrate 1 of his cases, it appears as if in addition to the distinct fracture dorsally in the tibia there is a line of fissure through the base of the medial malleolus.

In 1 of S. Franck's [66] cases he himself noted a fracture in the medial malleolus, and in 2 other cases it was according to his description not a fracture in the distal dorsal part of the tibia but a separation of the tibial epiphysis with a triangular diaphysial fragment which was torn from the tibia dorsolaterally, and thus an injury of a quite different nature.

According to this it must be considered doubtful whether any case of isolated fracture in the dorsal lip of the tibia has ever been found, and at any rate its existence seems not to be proved. Note Tanton's statement that it sometimes occurred in connection with fracture of the medial malleolus.

There is a difference of opinion about the genesis of the fracture involving the dorsal lip of the tibia. It has already been stated that

65. Walheim, T.: Intraarticular Malleolar Fractures, Acta chir. Scandinav. **79**:166, 1937.

66. Franck, S.: Solitary Fractures of Distal Edge of Tibia, Nord. med. **9**:643, 1941.

Rochet,[49] Lucas-Championnière,[51] Destot,[23] Chaput,[50] Meissner [54] and Backer Grøndahl [57] believed that the fracture was produced by forced plantar flexion of the foot, by which the talus would chip off the fragment. This view was accepted by Quénu,[22] Hilgenreiner,[63] F. de Quervain,[67] L. Böhler [68] and Clermont.[69] Thaon,[33] Tillaux,[32] Souligoux [58] and Bircher [55] believed that it originated from avulsion. Chaput [50] and Lane [70] expressed the opinion that both factors are instrumental. Schubert [71] assumed that the lateral malleolar fracture, after the oblique spiral fracture of the fibula had occurred, during its rotation and backward dislocation through pressure might affect the tuberculum posterius tibiae (Chaput) laterally and thus be instrumental in the production of the fracture in the dorsal part of the tibia.

In the review of my own experiments in a subsequent paper I shall revert to the discussion of the presumed isolated fracture of the lip of the tibia and the mechanism by which the fracture is likely to occur.

From the literature it appears that various forms of fractures in the dorsal part of the tibia have been found by roentgenography in a considerable percentage of the fractures of the ankle, but that opinions are divided on the pathogenesis and pathologic anatomy of this fracture. Some researchers have stated the belief that it is produced by chipping off, others that it is a tear fracture; some expressed the opinion that there is one form of fracture which involves the dorsal lip and the distal articular surface of the tibia and one form which is extra-articular, involving only the tuberculum posterius tibiae, while others have hinted that it is impossible to make a distinction between the two forms of fractures.

As far as I can see, fracture involving the dorsal lip of the tibia has not previously been the subject of experimental-surgical investigations.

Finally, the literature seems to show that its relation to syndesmotic rupture, diastasis and malleolar fractures has not been realized.

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67. de Quervain, F.: Spezielle chirurgische Diagnostik, ed. 4, Leipzig, F. C. W. Vogel, 1913, p. 714.

68. Böhler, L.: Die Verrenkungsbrüche im Sprunggelenk, Wien. klin. Wchnschr. **40**:104, 1927; Die Technik der Knochenbruchbehandlung, ed. 4, Vienna, W. Maudrich, 1936.

69. Clermont: Sur la disjonction tibio-péronière et les fractures du cou-de-pied (Essai de classification), Rev. de chir., Paris **47**:143, 1913.

70. Lane, W. A.: The Disastrous Results of Certain Abduction Fractures of the Ankle-Joint, M. Rev., London **24**:309, 1921; A Method of Treating Simple Oblique Fractures of the Tibia and Fibula More Efficient Than Those in Common Use, Tr. Clin. Soc. London **27**:167, 1894.

71. Schubert: Beiträge zur Kenntnis der Fussgelenkluxation durch Rotation nach aussen mit hoher Spiralbruch der Fibula, Deutsche Ztschr. f. Chir. **72**:396, 1904.

I have tried to solve these problems by experimental-surgical investigations.

(*b*) Fractures Involving the Anterior Lip of the Tibia: It has already been stated that a large number of authors (Cooper,[18] Malgaigne,[21] Richard,[39] Laborie,[26] von Volkmann,[27] Verneuil, Wagstaffe [72] and le Roy [31]) before the advent of the roentgenogram in clinical work had noted fracture with a small fragment torn off from the tibia anterolaterally.

Cases in which a large fragment had been torn from the anterior part of the tibia in connection with forward luxation of the talus were found at autopsy and operation by Nélaton,[47] Delmatte, Richard,[39] von Volkmann and Lauenstein.[73]

Thus Nélaton found a large fragment torn from the anterior part of the tibia in a young girl after a fall from the fourth story. C. Lauenstein found 4 cases of large fragment in connection with forward luxation of the talus after falls of 2 to 7 meters. These 4 cases were among a series of 1,000 fractures of the ankle. In 2 of Lauenstein's cases there was also malleolar fracture and in 2 other cases supramalleolar fracture. Lauenstein reported that the large avulsions from the interior lip of the tibia found by him were presumably of the same nature as the large fragment which von Volkmann had found anteriorly in the tibia in connection with forward luxation of the foot (fig. 6). This must be understood thus, that Lauenstein compared his cases with that of von Volkmann, about which the latter said that the line of fracture had a frontal course.

Experimentally fragments were produced anterolaterally in the tibia by Hönigschmied,[29] le Roy,[31] Stimson [36] and Quénu [22] by forced external rotation of the foot.

After the introduction of roentgenographic diagnosis it rather frequently occurred that a small fragment, and occasionally a large one, was torn from the tibia frontally.

Destot [23] found fragments frontally in the tibia in 35 of 1,700 fractures of the ankle. Of these 16 were large fragments. At autopsy he found a single case of a small fragment torn from the tibia anterolaterally in connection with bimalleolar fracture.

Chaput [30] recorded in 136 fractures of the ankle 12 cases of anterior fragment in the tibia (large in 4 cases and small in 8).

H. Hilgenreiner [63] thought that he had observed 2 cases of fracture in the anterior lip of the tibia. However, his oblique lateral roentgenograms show plainly that the lines of fracture pass through the basal

72. Wagstaffe: St. Thomas' Hosp. Rep. **6**:43, 1875.

73. Lauenstein, C.: Eine typische Absprengungsfraktur der Tibia, Deutsche Ztschr. f. Chir. **53**:477, 1899.

part of the medial malleolus and the adjacent part of the medial tibial diaphysis and not frontally in the tibia.

Meissner [54] reported that in 212 fractures of the ankle he found fracture in the anterior lip in 3 cases and in the lateral part of the tibia in 6. Of the anterior fragments two were small and one large (fig. 7). He stated that in one of these cases there was also a malleolar fracture. The lateral fracture in the tibia always occurred in connection with malleolar fracture.

Robert Jones [74] repeatedly found small fragments frontally in the tibia combined with malleolar fractures.

König [75] found small fragments at the anterior lip of the tibia in 2 patients with old fractures.

Grashey,[53] Medwin Leale,[76] F. de Quervain,[67] Clermont,[69] Tanton,[1] Svend Hansen [24] (fig. 8), Thore Walheim,[65] Husfeldt,[61], Nils Strømberg [77] and S. Franck [66] observed cases of small fragments torn from

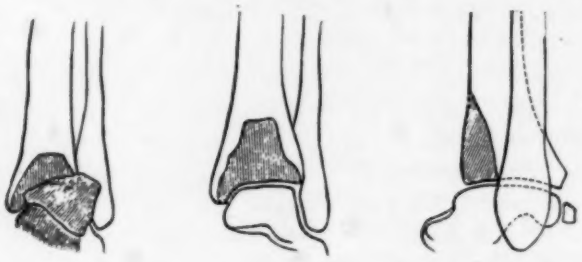

Fig. 6.—Lauenstein's illustration of the large fragment torn from the anterior lip of the tibia. Observation at operation before the advent of the roentgen ray.

the anterior lip of the tibia. They occurred partly isolated and partly together with malleolar fractures. Franck recorded that in 1 case by roentgen examination he found a large isolated fragment torn from the anterior lip of the tibia after a jump from the height of seven steps.

In Destot's [23] book on fractures of the ankle there is also an illustration of a large fragment from the anterior lip of the tibia. Auvray [78]

74. Jones, R.: On Fractures in the Neighbourhood of Joints, Lancet **2**:1479, 1910; An Orthopedic View of the Treatment of Fractures, Am. J. Orthop. Surg. **11**:314, 1918.

75. König, S.: Ueber Absprengungsfrakturen am vorderen und hinteren Abschnitt des distalen Endes der Tibia, mit Berücksichtigung der Rissfrakturen, Arch. f. klin. Chir. **99**:656, 1912.

76. Leale, M.: Fracture of the Anteroexternal Portion of the Lower Condyle of the Tibia Complicating Pott's Fracture, New York M. J. **94**:178, 1911.

77. Strømberg, N.: Results of Clinical-Roentgenologic After-Examination, Nord. med. (Hygiea) **3**:2957, 1939.

78. Auvray: A propos du fragment marginal postérieur das les luxations du pied en arrière, Bull. et mém. Soc. de chir. de Paris **38**:1107, 1912; A propos du traitement des fractures bimalléolaires vicieusement consolidées, ibid. **45**:1113, 1919.

found a similar case roentgenographically. Hatry [79] found 7 cases of large frontal tibial fragment combined with forward luxation of the talus in 1,830 fractures of the ankle.

In the works by Potherat,[80] John Dieterle,[81] A. Sachs,[82] Tanton,[1] F. Schnek,[83] Svend Hansen,[24] Matti [84] and Felsenreich [85] there are roentgenograms showing a large fragment torn from the anterior lip of the tibia.

Summary: Small fragments torn from the tibia anterolaterally have been found roentgenographically by many authors, partly as an isolated fracture and partly as a fracture combined with various forms of malleolar fractures. It is worth noting that this form of fracture is rarely stated to be found in connection with fractures of the ankle, that insufficient importance has been attached to the demonstration of these fractures, and that they have not been associated with the cases of ligamentous rupture, in spite of the fact that older researches (Cooper,[18] Malgaigne,[21] R. von Volkmann,[27] Stimson,[36] le Roy,[31] Quénu,[22] le Fort [20] and Hönigschmied [29]) found them uniformly pathologicoanatomically.

Fig. 7.—Meissner's illustration.

The reasons why they have so far been stated to be not of common occurrence are presumably that they are difficult to observe in the roentgenogram when they are small and therefore may be overlooked

79. Hatry: Bull. et mém. Soc. de chir. de Paris, July 3, 1912.

80. Potherat, E.: Fracture verticale de l'extremité inférieure du tibia, Bull. et mém. Soc. de chir. de Paris **35**:1296, 1911; Fractures malléolaires à type anatomique particulier, ibid. **38**:242, 1912.

81. Dieterle, J.: The Use of Kirschner Wire in Maintaining Reduction of Fracture Dislocation of the Ankle Joint, J. Bone & Joint Surg. **17**:990, 1935.

82. Sachs, A.: Ein seltener Fall von Tibiafraktur (Absprengungsfraktur aus dem distalen Ende der vorderen Tibiakant), Deutsche Ztschr. f. Chir. **75**:365, 1904.

83. Schnek, F.: Röntgendiagnostik der Knochenverletzungen, Vienna, Wilhelm Maudrich, 1932.

84. Matti, H.: Die Knochenbrüche und ihre Behandlung, ed. 2, Berlin, Julius Springer, 1931, p. 848.

85. Felsenreich, F.: Untersuchungen über die Pathologie des sogenannten Volkmannschen Dreiecks neben Richtlinien moderner Behandlungschwerer Luxationsfrakturen des oberen Sprunggelenkes, Arch. f. Orthop. u. Unfall-Chir. **29**:491, 1930-1931.

because they are overshadowed by thick bony parts and that they are inconspicuous as compared with other more dominating fractures in the malleoli by which they are frequently accompanied.

By the subsequent presentation of the results of my own experimental-surgical investigations and of my clinical material it will be shown that the avulsion of a fragment anterolaterally is an exceedingly frequent lesion in the various types of fracture of the ankle.

The large fragment torn from the lip of the tibia is discussed in the section "Pronation Dorsiflexion Fracture" in a subsequent paper.

2. *Rupture of the Syndesmosis—Diastasis.*—The word "diastasis" is used by older writers in the sense of increase of the width of the malleolar fork at fracture of one of the malleoli or at ligamentous rupture. From 1840 the word was employed in another sense. Thus Maisonneuve by "diastasis" understood the increase of the distance which

Fig. 8.—Svend Hansen's roentgenograms, both showing avulsion of a large fragment from the anterior lip of the tibia. There is a close resemblance to Lauenstein's illustration. Both show, too, avulsion of a small fragment from the anterolateral corner of the tibia in a fracture of the Pott type, which is a fracture of the same type as that illustrated by von Volkmann (compare figures 2 and 5).

occurs distally between the tibia and fibula when the ligament between them has been torn. Malgaigne [21] defined "diastasis" as luxation in a synarthrosis. Quénu [22] changed Malgaigne's definition by adding the word "permanent."

Within the field of experimental surgery Maisonneuve [14] was the first to show in which circumstances it may occur together with a high fibular fracture. He produced extensive ligamentous rupture distally between the tibia and fibula by external rotation of the foot, but he did not state in detail which ligamentous systems are ruptured, or the extent of the rupture. The same applies to subsequent authors who produced similar lesions by their experiments.

Eight years later Huguier [25] showed how diastasis is produced by apparently the same movement of the foot in combination with fibular fracture 3½ inches or more above the tip of the malleolus and with

ligamentous rupture at the medial malleolus. Hönigschmied [29] arrived by his experiments at the same result as Maisonneuve and Huguier.

Dunand [35] produced diastasis by external rotation of the pronated foot, after having cut the deltoid ligament.

Cooper [18] and Malgaigne [21] at autopsy ascertained inward luxation of the tibia in connection with fibular fracture 3½ inches above the tip of the malleolus and rupture of the interosseous ligament with a bony shell from the tibia anterolaterally. R. von Volkmann [27] at operation made observations similar to those stated by Cooper and Malgaigne. Richard [39] in a case of Pott's fracture ascertained diastasis and fragment from the posterior lip of the tibia.

Dupuytren [13] was the first to describe central luxation of the talus between the tibia and fibula in connection with a considerable diastasis. Later Schwartz,[86] Gangolphe,[87] Richet,[88] E. Gurlt,[48] W. Cheyne [89] and E. Braun [90] published cases of central luxation of the talus in connection with fibular fracture, exactly as Dupuytren had described this injury.

Ligamentous rupture and diastasis of a different nature was produced experimentally by le Roy [31] by external rotation of the foot. By his experiments he ascertained primary rupture of the ligamentum malleoli lateralis anterius. The rupture most frequently occurs at the tibial attachment of the ligament, but may also take place at the malleolar attachment, and always in connection with a small shell-shaped avulsion.

Stimson [36] showed by external rotation of the foot that the ligamentum malleoli lateralis anterius is torn from the tibial attachment with a bony shell and is followed by an oblique spiral fracture in the distal end of the fibula. Quénu [22] produced the same lesions as Stimson by external rotation of the supinated foot.

At autopsy in cases of total and partial forward luxation of the tibia Cooper [18] observed detachment of the ligamentum malleoli anterius with a bony shell, oblique spiral fracture in the fibula just above the lateral malleolus and fracture in the posterior lip of the tibia.

At operation R. Adams [38] observed backward luxation of the talus in connection with detachment of the ligamentum malleoli lateralis

86. Schwartz: Fracture de la malléole interne à sa base, Progres méd. **7**:671, 1879; cited by Quénu.[22a]

87. Gangolphe: De l'osteotomie dans le traitment des cas vicieux, Thesis, Lyon, 1882.

88. Richet, L. A.: Leçons cliniques sur les fractures du jambe, Paris, Ve. A. Delahaye & Cie, 1876.

89. Cheyne, W.: A Case of Old Fracture of the Fibula with Displacement of the Foot (Dupuytren's Fracture), Tr. Clin. Soc. London **27**:294, 1894.

90. Braun, E.: Luxatio pedis dextri cum diastasi ossium anticruris et ruptura ligamenti interossei, Hygiea **34**:363, 1872.

anterius from its tibial attachment and oblique fracture in the fibula just above the malleolus.

A third form of diastasis was produced by Tillaux [32] in his experiments. By abduction of the pronated foot he produced primary fracture in the medial malleolus and secondary rupture of the ligaments from the lateral malleolus to the tibia, which occurred with osseous avulsions *(fragment troisième)* from the tibial attachments of the ligaments (anterolaterally and posterolaterally).

Roentgenographically Chaput [50] proved diastasis in fractures of the ankle, as sometimes in the frontal roentgen exposure he found an increase of the distance between the tibia and fibula. The presence of diastasis is in his opinion proved when on the exposure *la ligne claire,* i.e., the clear space distally between the medial surface of the fibula and the tuberculum posterius tibiae, exceeds 3 mm. and when the distance between the contours of the medial surface of the fibula and the tuberculum anterius tibiae is less than 10 mm. Chaput stated that diastasis is present in 10 per cent of all fractures of the ankle.

Souligoux [58] and Destot [23] maintained in the beginning of the twentieth century that all fibular fractures which have their seat proximal to the talocrural joint are combined with diastasis and that the foot cannot be displaced laterally unless diastasis is found.

This caused Quénu [22] to make a thorough analytic investigation with a view to ascertaining the presence of diastasis in the different types of fractures of the ankle. It was as part of this work that he made his experiments by which he showed that by external rotation of the supinated foot the first lesion produced is detachment of the ligamentum malleoli lateralis anterius with a bony shell from the tibia and the second lesion is oblique spiral fracture in the distal end of the fibula just proximal to the lateral malleolus (that is to say, in contradistinction to Maisonneuve,[14] who stated that there is no diastasis at this fracture).

Quénu ascertained that when the ligament has been torn, diastasis will occur frontally between the tibia and fibula, by which the intermalleolar distance may be increased by 4 to 5 mm. The diastasis disappears spontaneously when the external rotation is removed before the fibular fracture occurs, but, if the latter fracture has once been produced, the diastasis will persist even though the rotation of the foot is discontinued.

By external rotation of the foot Quénu sometimes produced in addition to detachment of the aforementioned ligament a tear of the ligamentum interosseum tibiofibulare. In this case the diastasis will not fully disappear when the rotation of the foot is discontinued. Quénu reported that the ligamentum malleoli lateralis posterius is found to be intact on the said ligamentous ruptures in these experiments.

As stated before, Quénu defined diastasis as a permanent luxation in the synarthrosis between the tibia and fibula, and in his opinion it is only possible to speak of diastasis when a permanent increase of the distance between the tibia and fibula has been ascertained roentgenographically. It is the result of a sprain, a ligamentous rupture, just as luxation is the result of capsular rupture; diastasis, however, is not equal to a ligamentous rupture but is something more, as it implies an increased distance between the two bones.

In his opinion it is therefore incorrect to speak of diastasis in such cases if it has been present immediately on the trauma but if it has disappeared by manipulating the foot before the roentgen examination. He maintained that diastasis is comparatively rare and that Chaput's[50] estimate of 10 per cent of all cases of fractures of the ankle is far too high. He found diastasis only five times in 167 fibular fractures and twice in 58 tibial fractures. Furthermore, he maintained that diastasis is not constantly present in a certain type of fracture and that it is not a necessary condition for the production of any fracture. Finally, he maintained that diastasis may be present without any fracture at all.

Quénu concluded that diastasis may be found in widely different types of fractures: in the high fibular fracture, in the oblique spiral fracture in the distal end of the fibula and in fracture in the distal end of the tibia in such cases when it is combined with fibular fracture.

Destot [23] was of the opinion that diastasis is a far more frequent occurrence than is generally believed, and he and his pupil, Hassan-Fouad, expressed the opinion that they are able to prove that diastasis is present in all indirect fibular fractures on a level with or proximal to the talocrural joint. After having studied the normal anatomy of the distal tibiofibular articulation and the various forms of diastasis, Hassan-Fouad [91] tried to show that all the fractures found in the literature under the names "Dupuytren's fracture," "Tillaux' fracture" (abduction), "Maisonneuve's fracture" and "le Fort's fracture" are consequences of diastasis, as they cannot be produced by rotation of the fibula unless the ligaments between the tibia and fibula have been torn.

Destot [23] expressed the view that the small marginal fractures of the tibia occur in connection with rupture of syndesmotic ligaments, while the large avulsions at the posterior lip of the tibia do not involve the syndesmosis. Clermont [69] stated his belief that any form of marginal fracture of the tibia denotes lesion of ligaments in the distal tibiofibular articulation.

Svend Hansen [24] said in his thesis that a distinction should be made between total diastasis with complete disruption of the connection between the tibia and the fibula and partial diastasis in which the fibula distally remains anchored to the tibia by part of the ligaments

91. Hassan-Fouad: La dislocation mortaisienne dans les fractures du cou-de pied, Thesis, Toulouse, 1911.

between the bones; but otherwise, just like previous writers, he did not try to explain in which types of fractures of the ankle and to what extent rupture of ligaments and diastasis are found.

R. Merle d'Aubigne and Willy Smets [92] (1934) maintained that diastasis is present in approximately 20 per cent of all cases of fractures of the ankle and found that the best way of ascertaining diastasis is to state the ratio between the syndesmotic space (*la ligne claire*) and the distance between the two tubercula tibiae. This ratio is normally one third, and if it is found to exceed one half it denotes diastasis and lateral subluxation of the talus, especially if at the same time incongruity of the articular surfaces of the talocrural joint is found.

Ashhurst and Bromer (1922) reported that the best way of ascertaining diastasis is the determination of the ratio between the distance from the lateral surface of the fibula to the tuberculum anterius tibiae and the whole width of the fibular shadow measured on the same level. The ratio must not exceed two thirds.

Husfeldt [61] (1937) said in his work on rupture of the syndesmosis that he found that the methods of measurement for ascertaining diastasis given by Chaput,[50] d'Aubigne and Smets,[92] Ashhurst and Bromer [93] are not reliable; that he had tested them on 150 normal feet and found a considerable discrepancy between the results of the different methods.

On the other hand, Husfeldt found that the syndesmotic space (*la ligne claire*) in a normal foot never exceeds a width of 5 mm., and expressed the opinion that a syndesmotic space of 5.5 mm. or more always denotes diastasis. He also ascertained that if a roentgenogram is taken of both feet in the frontal plane at the same time, a difference of more than 1 mm. between the right and the left syndesmotic space will never be found, and from this he inferred that a difference of more than 1 mm. between the affected and the unaffected leg denotes syndesmotic rupture and diastasis.

From the literature it thus appears that in the experimental period the researchers succeeded in ascertaining a variety of ligamentous ruptures in the tibiofibular syndesmosis in fractures of the ankle by means of operations, autopsies and experiments, and that fairly soon after the advent of the roentgenogram changes were sometimes found around the syndesmosis which might be seen on the roentgenogram and which indicated rupture of its ligaments. Some authors tried to define the relationship between the marginal tibial fractures and syndesmotic rupture. It was observed that in the course of time various methods of measuring were proposed in order to ascertain whether syndesmotic rupture and diastasis are present. By closer examination it was grad-

92. Merle d'Aubigne, R., and Smets, W.: Les formes frustes de déplacement externe de l'astragale dans les fractures malléolaires, Presse méd. **42**:157, 1934.

93. Ashhurst, A. P. C., and Bromer, R. S.: Classification and Mechanism of Fractures of Leg Bones Involving the Ankles, Arch. Surg. **4**:51 (Jan.) 1922.

ually shown that these methods of measuring are not reliable roentgenographic criteria. Owing to the insufficiency of roentgenographic diagnosis in this field it is not possible to attain a reliable diagnosis of syndesmotic rupture and diastasis, which in turn causes widely different conceptions of the occurrence of syndesmotic ruptures.

In order to make clear which syndesmotic ligaments are torn in the different types of fractures of the ankle in their various stages and in order to ascertain the relationship between the tear of syndesmotic ligaments and the marginal tibial fractures I have made experimental-surgical and experimental-roentgenographic investigations, the results of which, given in a subsequent paper, will show that it is possible to make an exact diagnosis of ruptures of syndesmotic ligaments only when a genetic roentgenographic diagnosis can be made.

3. *Classification of Fractures of the Ankle.*—As, during the clinical and experimental periods, researchers did not manage to arrive at complete clarity and knowledge of the genesis and pathologic anatomy of all the malleolar fractures, they gave up, on the introduction of roentgenographic diagosis, the practice of classifying the fractures of the ankle according to their genesis and created classifications based on the pathologicoanatomic observations—the osseous lesions which could be found on the roentgenogram.

Quénu's [22] attempt in this respect was the first of a large number of classifications which have appeared up to the present day. He divided the fractures into the malleolar fractures proper (*portion genienne*) and the fractures which are situated above the malleoli either in one or both of the bones (*portion susgenienne*). Furthermore, he differentiated between isolated and associated fractures, and finally between fractures with and without diastasis. But as Quénu could not constantly ascertain diastasis in certain particular types of fractures, he thought that diastasis cannot form the basis of a classification of the fractures. His classification is exhaustive, but very diffuse and complicated, which made Ashhurst [60] characterize it as more a catalogue than a classification of the fractures of the ankle.

In addition to the pathologicoanatomic observations Destot [23] based his classification on a physiologic principle and differentiated between malleolar fractures proper and such fractures as are found in connection with marginal avulsions from the tibia and actual fractures in the dorsal part of the tibial articular surface.

He expressed the belief that these fractures give rise to lateral and dorsal displacement of the talus. Destot explained that in normal conditions the tibia, talus and calcaneus form a column of equilibrium which bears the weight of the body and transmits it to the foot. If this is changed by the slightest play in the malleolar fork, a gradual secondary valgus position with effacement of the plantar arch of the foot is caused. From this he concluded that the normal arch of the

foot is a function of the normal tibiofibular column of equilibrium and its transmission of pressure to the foot. The pressure of the column is normally transmitted to the talus in the fibular side of the main axis through the foot. If a certain play in the malleolar fork occurs by which the talus is subluxated laterally, the center of pressure of the column on the talus will shift medially on its upper surface, so that it will adopt a more medial position than is normal and perhaps be even tibial to the main axis of the foot. In this case the plantar arch of the foot will disappear. Therefore it is of great importance to the post-traumatic function of the foot that these luxations are fully eliminated in fractures of the ankle, and these lesions (marginal tibial fractures and diastasis) are of so great importance to the function of the ankle joint that there is full justification for taking them into account when classifying the fractures of the ankle.

Tanton [1] (1916) gave a third mode of classification by trying a combination of the principles of classification of Quénu and Destot. However, a clear classification which meant an improvement on that based on Quénu's and Destot's principles did not result from his work.

Pels Leusden [52] (1905) did not give an actual mode of classification, but called attention to the frequently occurring dorsal luxation of the foot in malleolar fractures and suggested the term luxation fractures for such conditions.

Grashey [53] (1907) in a long treatise reviewed the significance of roentgenographic diagnosis in relation to cases of fractures and explained what makes the fractures visible in the roentgenogram. He said of the oblique fracture distally in the fibula that the line of fracture commences frontally on a level with the talocrural joint, that it has an oblique course proximally and dorsally and that the proximal fragment is always found in close contact with the tibia, denoting that the ligamentum interosseum tibiofibulare is intact. He did not find isolated fracture in the posterior lip of the tibia, but often ascertained it in connection with malleolar fractures. On the other hand, he did find isolated fracture in the tuberculum anterius tibiae.

Meissner [54] (1909) divided the fractures of the ankle into adduction (supination) fractures and abduction (pronation) fractures, and it thus appears from the designation of the groups that he went back to a classification of the fractures of the ankle according to their genesis as indicated by the roentgenogram.

Meissner stated that in abduction fractures the primary lesion is fracture in the distal half of the lateral malleolus or just proximal to it and the secondary lesion is fracture in the medial malleolus. Inconsistently he recorded that in 5 of 25 adduction fractures there was an isolated fracture in the medial malleolus. He was not in agreement with what had previously been ascertained experimentally by several

authors when he reported fracture in the fibula proximal to the malleolus in adduction fractures.

In the abduction group the order which he gave for the lesions is: primary detachment of the deltoid ligament or fracture in the medial malleolus, secondary splitting off of the tip of the lateral malleolus or fracture in the fibula 5 to 8 cm. above the malleolar tip and tertiary rupture of the syndesmosis or osseous avulsion from the tibia anterolaterally. In spite of this statement he placed in this group isolated fracture in the lateral malleolus in 41 out of 126 cases. Furthermore, it should be noted that the order of the occurrence of the lesions in the abduction group is at variance with the results of the experimental-surgical investigations of several researchers by which primary fracture was produced in the medial malleolus, secondary interosseous ligamentous rupture, and tertiary fibular fracture more than 3½ inches above the tip of the lateral malleolus.

From the results of his classification it is evident how little he was aware of the results attained by experimental-surgical investigations with a view to the genesis of the fractures of the ankle.

Svend Hansen [24] applied to his material respecting fractures of the ankle a classification based on the pathologicoanatomic findings in the roentgenogram. He classified them into groups with isolated fracture in one malleolus, in both malleoli or in the lips of the tibia and groups with fractures in one or both malleoli in connection with marginal fractures of the tibia.

M. Henderson [94] (1932) also based his classification on the pathologicoanatomic findings (in the fractures demonstrated by the roentgenogram) in the following manner:

Isolated fracture of
- Medial malleolus
- Lateral malleolus
- Anterior lip of tibia
- Posterior lip of tibia

Bimalleolar fractures:
- Without luxation of talus
- With luxation of talus

Trimalleolar fractures

(The medial and lateral malleoli and the posterior lip of tibia, which because of its size is described as a third malleolus)

A great many authors (Pitha and Billroth,[95] F. König,[75] Georg Magnus,[96] Wilms and Wullstein,[97] H. Helferich, Heinrich Hilgenreiner,[63] M. Kirschner and G. Ellert,[98] F. Langenskiöld,[99] H. C. Slomann,[100]

94. Henderson, M. S.: Fractures of the Ankle, Wisconsin M. J. **31**:684, 1932; Trimalleolar Fractures of the Ankle, S. Clin. North America **12**:867, 1932; Fractures of the Ankle, Proc. Staff Meet., Mayo Clin. **6**:601, 1931.

*(Footnotes continued on next page)*

D. Nasse and M. Borchardt,[101] F. de Quervain,[67] Matti,[84] Frank Dickson,[102] and Backer Grøndahl [57]) divided the fractures of the ankle into supination (adduction) fractures, pronation (abduction) fractures and rotation fractures.

Others (Pels Leusden,[52] Lorenz Böhler,[66] F. Schnek [83] and E. Husfeldt [103]) applied the designations: supination (adduction) fractures, pronation (abduction) fractures and luxation fractures.

Husfeldt—an exception—tried in his work (1937) to state in which forms of fractures of the ankle there is diastasis, and his classification is cited here because it shows how he interpreted the pathologic anatomy of the different fractures of the ankle and their combination with syndesmotic rupture.

Husfeldt's classification is as follows:

A. Supination (adduction) fractures
  I. Fracture of lateral malleolus or ligamentous rupture
  II. I plus fracture of medial malleolus at the base or adjacent part or tibia; no diastasis
B. Pronation (abduction) fractures
  I. Fracture of the medial malleolus or rupture of the deltoid ligament
  II. I plus transverse fracture of the lateral malleolus below the syndesmosis or
    I plus syndesmotic rupture or
    I plus syndesmotic rupture and fibular fracture above the upper limit of the syndesmosis
C. Abduction and external rotation fractures
  I. Fracture of the medial malleolus or rupture of the deltoid ligament
  II. I plus oblique fracture of the fibula below the syndesmosis
  III. I plus rupture of the syndesmosis
  IV. I plus rupture of the ligamentum malleoli lateralis anterius and long oblique fracture through the syndesmosis
  V. I plus rupture of the ligamentum malleoli lateralis anterius and fibular fracture at the upper limit of the syndesmosis or in the upper third of the fibula

From this classification it appears that Husfeldt did not give any information as to which syndesmotic ligaments are torn or as to the occurrence of the marginal fractures of the tibia in association with syndesmotic rupture or in the various types of fractures of the ankle. This negative point of view with respect to these problems is found

95. Pitha, F. J., and Billroth, T.: Handbuch der allgemeinen und speciellen Chirurgie, Stuttgart, F. Enke, 1865-1880, vol. 4, pt. 2, p. 320.

96. Magnus, G.: Frakturen und Luxationen, Berlin, Julius Springer, 1937.

97. Wilms, M., and Wullstein, L.: Lehrbuch der Chirurgie, ed. 6, Jena, G. Fischer, 1919, vol. 3, p. 330.

98. Kirschner, M., and Ellert, G.: Fracturen, in Neue Deutsche Klinik, Berlin, Urban & Schwarzenberg, 1929, vol. 3, p. 493.

99. Langenskiöld, F.; Ingebrigtsen, R.; Kjærgaard, S., and Petrén, G.: Nord. lærebog i Kir. **3**:510, 1941.

100. Slomann, H. C.; Nicolaysen, J.; Petrén, G., and Rovsing, T.; Nord. Lærebog i Kir. **3**:741, 1922.

101. Nasse, D., and Borchardt, M.: Chirurgie der unteren Extremiteten, in von Bergmann, E.; von Bruns, P., and Mikulicz, J.: Handbuch der praktischen Chirurgie, Stuttgart, F. Enke, 1901, vol. 4, pt. 4, p. 444.

102. Dickson, F. D.: Fractures of the Ankle, J.A.M.A. **91**:845 (Sept. 22) 1928.

103. Husfeldt, E.: Significance of Roentgenography of Ankle Joint in Oblique Projection in Malleolar Fractures, Hospitalstid. **80**:788, 1937.

not only in Husfeldt but also in all the other authors from the entire roentgenographic period. Husfeldt's statements are also at variance with the results achieved by experimental-surgical research.

Only a slight knowledge of the results of the experimental period is traced both in the authors already mentioned and in the authors who later on in the roentgenographic period used the same or nearly the same nomenclature and who thus based their classification on the genesis of the fractures. No one tried to define precisely the roentgenographic or the pathologicoanatomic findings in the fractures in the various groups of classification. Most of the authors present explanations of the mechanisms of fracture; the statements given must, however, be presumed to be based on hypothetic reflections, as no experimental-surgical investigations are reported, as their records of the pathologicoanatomic conditions are scanty because it has only been possible to ascertain them occasionally by autopsy and as their knowledge of the results of the experimental surgery is slight, judging from the little consideration which the various authors give this aspect of the matter and from the substantial discrepancy between their conceptions and the results of the experiments.

It meant only a slight improvement that these authors in order to support their classification attached historical names such as Pott, Dupuytren, Maisonneuve, Destot, Lauenstein and Volkmann to the fractures of the various groups, since the pathologicoanatomic conditions and the roentgenogram of the fractures which bear these names were not at all uniformly determined. To exemplify this it may be stated that Pott, who described a particular type of fracture, and Dupuytren have had their names attached to the same form of fracture. Besides, Dupuytren's name is often used to designate three different forms of ankle lesion: malleolar fracture combined with central luxation of the talus, the fracture described by Pott (*fracture Dupuytren type*) and the oblique spiral fracture produced experimentally and described by Maisonneuve (*"fracture Dupuytren basse"*). The designation Pott's fracture is also sometimes applied to these fractures. Volkmann's triangle is used to designate fractures both in the anterior and in the posterior lips of the tibia, although von Volkmann described only an osseous lesion in the anterior part of the tibia. Therefore it is comprehensible that authors who divided the fractures of the ankle into adduction, abduction and rotation fractures, or into adduction, abduction and luxation fractures, in their classifications often arrived at widely different results depending on the individual judgment as to which fractures should belong to the various groups of fractures.

The consequence of this was some confusion and almost chaos in the field of fractures of the ankle, which made it impossible to differentiate the fractures into groups the pathologic anatomy of which was exactly determined, the treatment (reduction and retention) of which

could be outlined and the prognosis of which could be made with some amount of certainty.

A work published by Ralph G. Carothers [104] in 1941 seemed to indicate that the thought of creating a classification based on a thorough understanding of the various forms of fractures of the ankle had been completely abandoned. He proposed merely to classify the fractures of the ankle according to the displacement of the talus.

Ashhurst and Bromer's [93] significant and epoch-making work published in 1922, which will be reported later in this paper, forms an exception to what has been said here about the classifications of fractures of the ankle by the authors of the roentgenographic period. It has, however, not been appreciated according to its merits, as their principles of classification of fractures of the ankle have been employed only by Bishop and Thore Walheim.[65]

Ashhurst and Bromer recommended that attempts be made to create a classification which could assemble the fractures of the ankle in a few, fairly well defined groups. They found that the best course to adopt was to classify the fractures according to the genesis when that which previous researchers and they themselves had ascertained by experimental surgery concerning fractures of the ankle was made the basis of the classification. They expressed the belief that such a classification, imperfect though it may be owing to lack of knowledge of the mechanism of several fractures of the ankle, would give some clarity in the prevailing chaos, so that it would be easier to remember and understand the details of the complicated lesions of the ankle and to plan the treatment of the individual groups of fractures. They reported having made experimental-surgical investigations with a view to the production of fractures, but did not state in detail how the experiments were carried out, what they aimed at or what they resulted in, which justifies the presumption that they found nothing new.

Their classification of 300 fractures of the ankle is as follows:

| | | |
|---|---|---|
| **Fractures by adduction (tibial flexion)** | | |
| First degree: Fracture of lateral malleolus—transverse—at or below level of distal articular surface of tibia (tibial plafond) | 27 | (9%) |
| Second degree: First degree plus fracture of medial malleolus | 11 | 3.6% |
| Third degree: First degree plus supramalleolar fracture of tibia | 2 | 0.66% |
| | 40 | 13.3% |
| **Fractures by abduction (fibular flexion)** | | |
| First degree: Fracture of medial malleolus | 20 | 6.6% |
| Second degree: First degree plus fracture of fibula (transverse, just above or below distal articular surface of tibia) | 41 | 13.7% |
| (Below distal articular surface of tibia) 13 | | |
| (Above the syndesmotic connection between tibia and fibula, with diastasis) 28 | | |
| Third degree: Medial malleolus represented by distal end of tibia | 2 | 0.66% |
| | 63 | 21% |

104. Carothers, R. G.: Classification of Ankle Fractures Based upon Pathology and Indications for Treatment, Surg., Gynec. & Obst. **72**:410, 1941.

| | | |
|---|---|---|
| Fractures by external rotation | | |
| First degree: Oblique fracture of distal end of fibula | 79 | 26% |
| Second degree: First degree plus fracture of medial malleolus or rupture of its ligaments (55 cases complicated by fracture in posterior lip of tibia) | 100 | 33% |
| Third degree: First degree plus supramalleolar fracture of tibia | 5 | 1.7% |
| | 184 | 61% |
| Isolated fracture in the posterior lip of tibia | 1 | |
| Comminution of distal articular surface of tibia | 3 | |
| T or Y fractures in distal end of tibia (Gosselin) | 8 | 2.7% |
| Fractures by direct violence | 5 | 1.7% |

From Ashhurst and Bromer's classification it appears that the fractures of the ankle are presumed to be due to adduction, abduction and external rotation.

According to them the adduction fractures cannot give rise to discussion, as their genetic mechanism has been explained by so many researchers in experimental surgery.

They expressed the opinion that the abduction fractures occur in conformity with the experiments carried out by Bonnet,[20] Hönigschmied[29] and Tillaux,[32] which showed that they could be produced experimentally with primary fracture in the medial malleolus and secondary in the fibula.

Their classification of the clinical fractures shows that they supposed that the fibular fracture in this group may be situated partly below, partly above the talocrural joint, and even in the proximal end of the fibula. That the fibular fracture in some cases is localized below the distal articular surface of the tibia is at variance with Tillaux' experimental results, which showed that after detachment of the ligaments between the tibia and fibula the fibular fracture was always proximal to the talocrural joint. That the fibular fracture by forced abduction is often supposed to occur proximal to the syndesmosis in association with diastasis, is at variance with other experimental-surgical results, since Maisonneuve,[14] Huguier[25] and Hönigschmied[29] produced fracture in the fibula 3½ inches or more above the tip of the malleolus in association with diastasis, but only by external rotation of the foot.

In Ashhurst and Bromer's opinion the oblique spiral fracture in the distal end of the fibula is an external rotation fracture, which occurs by external rotation of abducted and pronated foot when the interosseous ligaments between the tibia and fibula are not torn. From this it will be seen that they, like all other authors, presumed that the spiral fracture distally in the fibula is a pronation fracture.

That this fracture in Ashhurst and Bromer's opinion is produced by rotation is in agreement with the results achieved by Maisonneuve, Hönigschmied, le Roy,[31] Stimson[36] and Quénu.[22] However, Ashhurst and Bromer had not noted, or presumably did not know, Quénu's experiment since they did not mention it. Quénu showed, as has already been reported, that by external rotation of a supinated foot the

primary lesion was detachment of the ligamentum malleoli lateralis anterius with a bony shell torn from the tibia anterolaterally and the secondary was an oblique spiral fracture in the distal end of the fibula. It also seems as if Ashhurst and Bromer had not noted that Stimson and le Roy in their experiments by forced external rotation of the foot primarily produced detachment of the ligamentum malleoli lateralis anterius with a bony shell and secondarily the distal oblique spiral fracture in the fibula.

In Ashhurst and Bromer's opinion the ligamentum malleoli lateralis anterius, which is attached to the least proximal half of the lateral malleolus and which is a taut ligament that allows of lateral movement of the malleolus to the extent of only a couple of millimeters, is intact in the great majority of cases of oblique spiral fracture in the distal end of the fibula. They reported, however, that the line of fracture in the roentgen picture commences anteriorly in the bone on a level with the talocrural joint and that it runs from there in a dorsal-proximal direction.

The pestle-shaped lateral malleolus, to the proximal half of which the ligamentum malleoli lateralis anterius is attached, does not reach further proximally than the talocrural joint, which shows that Ashhurst and Bromer were inconsistent when they alleged that the oblique spiral fracture in the distal end of the fibula is produced by rotation and without lesion of the ligamentum malleoli lateralis anterius, at the same time stating that the line of fracture commences in the fibula level with the talocrural joint; i. e., proximal to the attachment of the ligament to the malleolus. One of these statements must accordingly be wrong.

The fibular fracture proximal to the ligamentum malleoli lateralis anterius cannot be produced by rotation as long as the ligament is intact and anchors the lateral malleolus to the tibia.

If the fibula is fractured distal to the ligamentous attachment to the lateral malleolus, the line of fracture cannot be situated as Ashhurst and Bromer said that it is in the roentgen picture.

In a subsequent paper it will be demonstrated that their indication as to the seat of the fracture in the roentgenogram must be supposed to be correct, whereas their assumption that the ligamentum malleoli lateralis anterius is intact must be presumed to be hypothetic and incorrect. The same applies presumably to their conception of the production of this fracture by forced external rotation of the pronated and abducted foot.

They did not introduce fracture in the posterior lip of the tibia as a feature of the mechanisms of fractures of the ankle, but cited it only as a complication in various forms of fractures. They mentioned nothing new about this form of fracture, but contented themselves with ascertaining, as so many authors had done before them, that it is frequent and that it is found in one quarter of all fractures of the ankle.

Thus Ashhurst and Bromer were in disagreement on some points with the results achieved by older researchers by experimental surgery; yet it does not appear from their work that they had obtained results differing from those of earlier researchers in their experiments.

Besides, the weak points of Ashhurst and Bromer's classification are conspicuous because several essential problems (the marginal fractures of the tibia and syndesmotic ruptures) are not included in their system of classification.

This is presumably the reason why their system of classification has not been used so much in spite of the considerable and epoch-making value of this work, which without doubt meant a first and important step toward the formation of a surveyable and rational classification of the fractures of the ankle according to their genesis as interpreted in the roentgenogram.

It will be seen from the results of my own experimental-surgical and experimental-roentgenographic investigations and clinical studies how it is possible to produce all fractures of the ankle experimentally, to ascertain their pathologic anatomy and to make determinations from roentgenograms and thus obtain a complete genetic classification.

4. *Reduction and Retention of Fractures of the Ankle.*—From these reports it is seen that in both the clinical and the experimental periods great importance was attached to obtaining the best possible reduction of luxation and fracture in lesions of the ankle.

During the clinical period reduction was performed on the extended extremity and sometimes by violent traction. Toward the end of this period Pott [8] introduced semiflexion, by which a gentler reduction became possible. In the period from Pott to Dupuytren [13] surgeons seemed to have tried in a more rational way to direct their treatment toward the lesion—the fibular fracture—to which they thought the deformity of the ankle joint and the traumatic flatfoot after luxation of the talocrural joint were due.

Yet it was not until the experimental period, after it had been possible by means of experimental surgery to arrive at a closer knowledge of the pathologic anatomy of certain types of fractures, that Dupuytren from his great knowledge of the mechanisms of fractures of the ankle could form his mechanism of reduction and his splint. He reduced the fracture by supinating, adducting and plantar flexing the foot.

However, from about 1840 it was maintained that Dupuytren's splint could not maintain the reduction so that post-traumatic external rotation and backward displacement of the foot could be avoided. Therefore Maisonneuve supplemented Dupuytren's splint with a dextrin dressing, and Malgaigne replaced it by a plaster cast. Gradually these methods of splinting, too, proved their insufficiency, as deformity of the foot and traumatic flatfoot, which impaired the gait essentially, were still frequently the consequences of fractures of the ankle. In the last

quarter of the nineteenth century the Americans Gordon Buck and Crossby try to maintain the reduction by means of extension. In Europe this mode of treatment was subsequently instituted by J. Hennequin (France),[105] R. von Volkmann [27] and von Bruns [106] (Germany). B. Bardenheuer [107] was the first to introduce systematic treatment with permanent extension. He developed this well known mode of reduction into a mode of retention.

From the end of the experimental period and throughout the roentgenographic period the commonest treatment of by far the greatest number of fractures was manual reduction and retention of the fracture either by a plaster cast or by permanent extension. Splinting of the foot in maximal dorsiflexion was introduced, but otherwise with adducted and supinated foot as stated by Dupuytren. Thereby Dupuytren's treatment was essentially modified, perhaps more than has so far been realized.

Some authors have warned against too marked adduction and supination of the foot because thereby the lateral malleolus together with the fragment of the posterior lip of the tibia may be displaced (Destot [28]), because the fragment of the lateral malleolus may thereby be removed too much from the proximal fragment of the fibula, by which the osseous healing is delayed (Bliesener [108]), or because overcorrection may result in permanent varus position and marked thickening of the lateral malleolus (Bähr,[109] F. Lange,[110] Colvin [111]). Oberst [112] and Wendt laid the greatest stress on the reduction of the lateral subluxation and recommended splinting in a middle position. The same applied to E. J. Lloyd [113] and L. Böhler,[68] who maintained that it is a mistake to place the anterior part of the foot in marked adduction and supination. In their opinion the posterior part of the foot should be

105. Hennequin, J., and Loewy, R.: Les fractures des os longs; leur traitement pratique, Paris, Masson & Cie, 1904.

106. von Bruns: Die Lehre von den Knochenbrüchen, Stuttgart, Ferdinand Enke, 1887.

107. Bardenheuer, B.: Die allgemeine Lehre von den Frakturen und Luxationen, mit besonderer Berücksichtigung des Extensionsverfahrens, Stuttgart, Ferdinand Enke, 1907.

108. Bliesener: Ueber die durch die Bardenheuer'sche Extensionsmethode an den Brüchen der unteren Gliedmassen erhaltenen funktionellen Ergebnisse, Deutsche Ztschr. f. Chir. **60**:277, 1900.

109. Bähr, F.: Fractura malleoli interni non sanata, Deutsche Ztschr. f. Chir. **119**:479, 1912.

110. Lange, F.: Die Behandlung der Knochenbrüchen durch den praktischen Arzt auf Grund orthopädischer Erfahrungen dargestellt, München. med. Wchnschr. **72**:949, 1925.

111. Colvin, A. R.: Fracture of the Lower Ends of the Tibia and Fibula, Surg., Gynec. & Obst. **18**:99, 1914.

112. Oberst: Monatschr. f. Unfallsheilk. **14**:219, 1907.

113. Lloyd, E. I.: Fractures Round the Ankle Joint, Brit. M. J. **2**:1286, 1939.

slightly adducted, but if the anterior part of the foot is not to be splinted in a middle position it must be done in slight pronation and absolutely not in supination.

In addition to tight-fitting plaster casts, many other forms of plaster cast were gradually introduced, such as von Brun's plaster cast with a walking iron attachment, plaster cast ad modum Paris, plaster *gouttière* (Clermont [69]) and various other walking plaster casts (Tscherning [114] and Többen) and Lexer's [115] dressing splint.

Just like the plaster casts Bardenheuer's [107] treatment with permanent extension was also modified in various ways. Bardenheuer himself applied extension by means of strips of adhesive tape on the extended extremity. Zuppinger [116] constructed an apparatus for automatic extension. Codivilla [117] used nail extension, and later wire extension was introduced, which has gradually come into common use. Zuppinger, Kümmel and Wessel modified the extension treatment by applying the traction to the more or less flexed extremity.

In spite of the aid of roentgenology in the establishment of the number of fractures and of luxations and dislocations in the individual cases these methods of treatment did not prove so successful that fractures of the ankle ceased to be a problem. Disability following fracture of the ankle is still common, and roentgenographic after-examinations show that in addition to valgus position of the talus arthritic changes are found, and often dorsoproximal displacement of the fragment of the posterior lip of the tibia with a jutted formation on the distal articular surface of the tibia is found. Therefore the treatment aims especially at a complete reduction of the posterior lip of the tibia. Extension treatment is applied to dislocation of this fragment, attempts being made by means of nails or wire through the calcaneus to exercise a safe and powerful traction. By this change of the extension treatment the principle of therapy of severe lesions of the ankle becomes to some extent that employed in the clinical period for severe luxations of the ankle joint, since the permanent extension is now changed from being a pure retention treatment to a method which also comprises reduction. This application of extension to cases of severe fractures of the ankle with avulsion of large tibial fragments came gradually into wide use.

By this treatment L. Böhler [68] and F. Felsenreich [85] adopted an exceptional position toward fracture of the ankle with a large fragment torn from the posterior lip of the tibia. L. Böhler expressed the

114. Tscherning, E. A.: Spadserebandager, Bibliot. f. læger **6**:38, 1895.

115. Lexer, E.: Zur Behandlung der Knochenbrüche, München. med. Wchnschr. **56**:593, 1909.

116. Zuppinger, H.: Ueber Torsionsfrakturen speciell des Unterschenkels, Beitr. z. klin. Chir. **27**:735, 1900; Automatische wirkende Apparate zur permanenten Extensionen, Zurich, 1908.

117. Codivilla, A.: Sur una méthode de traction appliquée directement au squelett; extension par le clou, Assoc. franç. de chir. Proc.-verb. **23**:763, 1911.

opinion that extension by wire traction alone does not suffice to secure complete reduction in these fractures, but that this can be obtained only by screw traction. This method has been used to a certain extent, and good results have been reported, especially by Böhler himself.

After having applied the screw traction method for some time, F. Felsenreich declared that it is insufficient for the retention of a large fragment from the posterior lip of the tibia. He therefore combined it with his own conservative operative method, percutaneous nailing in order to secure the retention of the fragment from the posterior lip of the tibia.

In spite of the fact that treatment of fractures of the ankle by these methods and by roentgen control has improved to a great extent, the results having improved considerably as compared with previous results, follow-up examinations of great numbers of patients at various times in this century have shown that a considerable percentage of patients with fractures of the ankle suffer from a varying degree of permanent deformity, sometimes amounting to disability. This is exemplified by several publications (Jottkowitz,[118] Haenel,[119] Ramsperger,[120] Sonntag,[121] Molineus [122]).

I shall not go into a detailed review of these works, but shall be content to mention, by way of example, that Borchardt [123] (1914), judging from the results of various follow-up examinations from the beginning of the twentieth century, estimated that 25 to 30 per cent of all the patients suffered from permanent deformity from their fractures of the ankle and that Svend Hansen [24] (1919) found disability in 20.8 per cent of 226 fractures of the ankle.

Follow-up examinations cited both from the beginning of this century and from the last decade show that the results of treatment are not fully satisfactory, and therefore it can be understood that surgeons of this century at intervals right up to the present day have tried to work out operative methods and have recommended their application to such fractures as experience shows will result in disability. Very early operation on fresh fractures of the ankle was proposed by Bland-

118. Jottkowitz, H.: Ueber Heilungsresultate von Unterschenkelbrüche mit Bezug auf das Unfallversicherungsgesetz, Deutsche Ztschr. f. Chir. **44**:610, 1896.

119. Haenel, F.: Ueber Frakturen mit Bezug auf das Unfallsversicherungsgesetz, Deutsche Ztschr. f. Chir. **38**:129, 1893-1894.

120. Ramsperger: Ueber die Heilungsdauer der Unterschenkelbrüche bis zur Wiederherstellung der endgültigen Arbeitsfähigkeit, Med. Cor. Bl. d. württemb. ärztl. Ver. **66**:345 and 353, 1896.

121. Sonntag, E.: Unterschenkelbrüche mit Bezug auf das Unfallversicherungsgesetz, Bonn, E. Eisele, 1904.

122. Molineus: Ueber das Endresultat bei doppelten Knöchelbrüchen, Deutsche Ztschr. f. Chir. **120**:137, 1912.

123. Garrè, C., and Borchardt, A.: Lehrbuch der Chirurgie, ed. 8, Leipzig, F. C. W. Vogel, 1935, vol. 2, pp. 621-626.

Sutton,[124] Lane,[70] Richet,[88] Lambotte,[125] Bauer,[126] Dujarier[127] and Lounsbury.[128] Lambotte[125] is the most eager advocate of primary operation according to wide indications. As recently as 1940 he maintained that permanent extension is only a ridiculous further development of a mode of treatment described by Galen; that manual reduction as it is still used is that stated by Dupuytren, and that these methods cannot fulfil modern requirements of the therapy of fractures of the ankle. He advocated primary operation in case of luxation or dislocation.

Numerous surgeons—perhaps the majority—nowadays partly follow Lambotte and perform operative reduction, when manual reduction does not lead to anatomically correct position, and a great many good results have been reported (by Moffat,[129] K. Ludloff,[130] A. Beck,[131] M. E. Juvara,[132] Greef,[133] Geston Picot,[134] Cornioley,[135] R. Ollerenshaw,[136] Jean Gattelier, Henri Hartmann,[137] Henry Platt,[138] R. P. Rowlands[139] and Abraham Troel.[140]

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124. Bland-Sutton, J.: Fracture of the External Malleolus, Lancet **1**:714, 1914.

125. Lambotte, M. A.: Quelques considerations sur le traitement des fractures malléolaires, Bull. Acad. roy. de méd. de Belgique **6**:472, 1938.

126. Bauer: Hospitalstid. **4**:1120, 1911.

127. Dujarier, C.: Traitement sanglant des fractures de jambe récentes, Thesis, Paris, no. 211, 1900; Traitement des fractures anciennes de Dupuytren, vicieusement consolidées, Bull. et mém. Soc. de chir. de Paris **45**:984, 1919.

128. Lounsbury, B. F., and Metz, A. R.: Lipping Fracture of Lower Articular End of Tibia, Arch. Surg. **5**:678 (Nov.) 1922.

129. Moffat, B. W.: Bimalleolar Fractures, J.A.M.A. **90**:690 (March 3) 1928.

130. Ludloff, K.: Die Wiederherstellung der normalen Knöchelgabel, Deutsche Ztschr. f. Chir. **225**:321, 1930.

131. Beck, A.: Zur Frage der operativen Behandlung der Luxationsfrakturen des Fussgelenkes, Deutsche Ztschr. f. Chir. **228**:289, 1930.

132. Juvara, M. E.: Traitement osteosynthétique des fractures des malléoles simples du compliquées de diastasis du péroné, Bull. et mém. Soc. de chir. de Paris **21**:34, 1929.

133. Greef: Blutige Behandlung der Knochenbrüche, Deutsche med. Wchnschr. **53**:508, 1927.

134. Picot, G.: Fractures bimalléolaires avec fragment marginal postérieur, Bull. et mém. Soc. de chir. de Paris **48**:1086, 1922; L'intervention sanglante dans les fractures malléolaires, J. de chir. **21**:529, 1923.

135. Cornioley: Dans quelles conditions faut-il opérer les fractures graves du cou-de-pied (genre Dupuytren), Lyon chir. **26**:305, 1929.

136. Ollerenshaw, R.: Observations on Treatment of Fractures Involving the Ankle Joint, Brit. M. J. **1**:585, 1929.

137. Hartmann, H.: A propos du traitement des fractures de Dupuytren (M. Boppe and Vassitch service de traumatologie-d'Hôtel-Dieu), Bull. et mém. Soc. nat. de chir. **55**:247, 1929.

138. Platt, H., and others: Introduction to a Discussion on Fractures in the Neighborhood of the Ankle-Joint, Lancet **1**:33 and 90, 1926.

139. Rowlands, R. P.: Fracture-Dislocations of the Ankle: Pott's and Dupuytren's Fractures, Brit. M. J. **2**:735, 1919.

140. Troel, A., cited by Ingebrigtsen, R.; Kjærgaard, S., and Petren, G.: Nord. lærebog i kir. **1**:422, 1941.

In a subsequent paper I shall review the results of my own experimental-surgical investigations and of genetic reduction of fresh clinical fractures in order to show how it is possible to perform a genetic reduction in conformity with the actual nature of the individual type of fracture.

If a brief summary of the results of the various research periods is to be given, the following points may be emphasized:

During the clinical period it becomes increasingly obvious that the fibular fracture is a very frequent—perhaps a constant—complication in luxations of the talocrural joint.

During the experimental period it was gradually ascertained that luxation of the talocrural joint is not only always accompanied by fracture of the lateral malleolus or of the fibula, but also frequently accompanied by fracture of the medial malleolus and by diastasis between the tibia and fibula and that several widely different forms of fractures of the ankle exist, which according to experimental-surgical investigations are produced by varying mechanisms of fracture.

During the roentgenographic period the correctness of the conception formed in the experimental period has been borne out; it has been shown that fractures of the dorsal lip of the tibia are much more frequent than had so far been suspected, and that anterolateral fracture of the tibia and diastasis distally between the tibia and fibula are not at all rare.

Attempts are made to develop and improve the methods of treatment gradually as the knowledge and understanding of the nature of the various forms of fractures are increased.

In spite of extensive application of roentgen examinations with a view to diagnosing fractures of the ankle and exploring their nature the problem of fractures of the ankle is far from having been solved.

It may then be pointed out that even though the roentgenology has contributed essentially to throwing light on the multiplicity of fractures of the ankle and has added to the precision of diagnosis, by which improved results of treatment became possible, it has not provided the exact and detailed diagnosis which must be the aim.

## CONCLUSIONS

1. The exact genesis of most fractures of the ankle is still unknown.

2. The problem of the relationship between the marginal tibial fractures and the malleolar fractures and between the former and rupture or detachment of syndesmotic ligaments has not been solved.

3. A sure knowledge of rupture or detachment of the ligaments of the syndesmosis in the various types of ankle fractures has not been reached.

4. The criteria of rupture or detachment of syndesmotic ligaments are uncertain.

5. The classification of the malleolar fractures in the literature is almost chaotic.

6. No attempts have been made to reduce the malleolar fractures in conformity with their actual nature.

Many roentgenographic studies and experimental surgical and clinical investigations have been made in the course of time, but have not provided the final solution of these problems of fractures of the ankle.

In my studies of and experiments with malleolar fractures I combined experimental-surgical and experimental-roentgenographic investigations in order to solve the problem by attaining an exact knowledge of: (1) the origin (mechanism, genesis) of all fractures of the ankle; (2) the pathologic anatomy of all fractures of the ankle—also as far as marginal fractures of the tibia and rupture or detachment of syndesmotic ligaments are concerned; (3) the characteristic roentgen picture of all fractures of the ankle—genetic roentgenographic diagnosis, and (4) the mode (mechanism) of reduction—genetic reduction—of all fractures of the ankle.

By this method of examination four types of fractures of the ankle were found. Each of them has its own particular genesis and occurs in from two to four stages, which is constant in the individual type of fracture.

By the study of roentgenograms from 229 patients it was proved that it was possible to determine the origin (genesis) of all fractures of the ankle, their pathologic anatomy and their genetic roentgen diagnosis, and by this it was ascertained that the types of fractures of the ankle produced by experimental surgery correspond to 99 per cent of the clinical fractures.

That it is possible to determine the genetic reduction by experimetal-surgical investigations was borne out by performing—after genetic roentgen diagnosis—genetic reduction of fresh fractures of the ankle to anatomically correct positions.

In a subsequent paper it will be explained how these results were achieved.

# SYNTHETIC RESIN—A NEW ANTACID FOR TREATMENT OF PEPTIC ULCER

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SINCE the invention of "celluloid" by Hyatt in 1869 the synthetic plastics industry has extended so widely that it touches on almost every sphere of science and industry. Synthetic plastics, such as acrylics, "vinylite," "cellophane," "nylon" and "bakelite" [1] are now employed as surgical appliances, instruments, sutures and dressings, but the plastics have not been used in clinical medicine. We are now studying a plastic substance commercially known as "amberlite IR IV," a synthetic resin which is chemically allied to "bakelite," and in this paper [2] will describe its effect on peptic ulcer.

## DESCRIPTION OF RESINOUS PLASTICS

Natural resins have been known and used since antiquity. Miastic and storax, natural resins, were employed by the Egyptians in preserving their mummies, and frankincense, a natural resin, was among the gifts of the Magi to the Infant Jesus. During the Renaissance, Rembrandt and Da Vinci were known to have improved their paintings with the use of amber, another natural resin, in their varnish. Since that time natural resins have found increasing use in various industries, particularly in those industries which are now classified as "plastics producers," i. e., paint, rubber, asphalt, "celluloid," glue and gelatine.

Synthetic resins which bear a physical resemblance to natural resins were evolved from the studies of Adolph von Baeyer in 1872 but were

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From the Presbyterian Hospital.

Read in a symposium on Peptic Ulcer before the joint meeting of the Section on Surgery, General and Abdominal, and the Section on Gastro-Enterology and Proctology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, June 1947.

1. Ingraham, D.; Alexander, E., and Watson, D. D.: Synthetic Plastic Materials in Surgery, New England J. Med. **236**:362 (March 6); 402 (March 13) 1947.

2. The resin used in this study was supplied through the courtesy of Mr. Steven Horoschak, Research Department, National Drug Company, Philadelphia.

not put to practical use until L. H. Baekeland in 1909, by the employment of heat, transformed a phenol-formaldehyde condensation product into an infusible, insoluble substance, resin-like in character, which is known by the name of "bakelite." This discovery started the vast synthetic resin industry, and phenol-formaldehyde condensation products of various types have in the past twenty-five years been used as substitutes and hardeners for natural rubber, shellac, asphalt and "celluloid."

Prior to 1935 the criterion of a synthetic resin's worth was the physical properties which it imparted to a finished product such as a brush handle or radio panel. In that year Adams and Holmes [3] discovered that phenolic resins had ion exchange properties. Their discovery started a revolution in the chemical world. It now became possible to remove both acids and alkalis from solutions without changing the nature of the original solvent. By consecutive use of phenolic and amino resins it became possible to effect complete removal of dissolved salts from a solution, leaving a filtrate equivalent to distilled water. It seemed inevitable that such substances, since they were nontoxic for human beings, would eventually find a place in medicine. In 1938 one of us (M. K.) discussed with Mr. Howard Tiger, who was working with the new resins in the water-softening industry, the use of these anion exchangers for treating peptic ulcer. We computed that the resins then available had such poor acid-binding qualities that they would have to be ingested in quantities which would render their use impractical.

## THE USE OF ANTACIDS FOR PEPTIC ULCER

The use of antacids in the therapy of peptic ulcer has developed during the latter half of the life of the American Medical Association. The treatment of gastric ulcer with a mixture of bismuth subcarbonate and sodium bicarbonate was started in Europe in 1895 by von Strumpell, and Bertram Sippy, of Chicago, in 1915 specifically recommended antacids for the more common duodenal ulcer. Sippy originally prescribed bismuth subcarbonate, sodium bicarbonate and magnesium oxide and later calcium carbonate. In 1923 John Kantor, of New York, advised the use of the tertiary phosphates of magnesium and calcium instead of Sippy's powders because the latter frequently brought on a state of alkalosis. Since all these metallic salts had deficiencies, attempts have been made during the past twenty years to improve on the antacids in use. Various mixtures of antacids have been tried. The introduction of aluminum hydroxide and phosphate and magnesium trisilicate in the 1930's was the result of an effort to overcome some of the faults inherent in the alkalis used by Sippy and Kantor.

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3. Adams, B. A., and Holmes, E. L.: Adsorbtive Properties of Synthetic Resins, J. Soc. Chem. Indust., Jan. 11, 1935, p. 1 T.

### DISADVANTAGES OF THE COMMON ANTACIDS

The chief disadvantages of the commonly employed metallic salt antacids follow:

1. The salts of aluminum, bismuth and calcium are constipating.
2. The salts of magnesium are laxative and cause perianal burning.
3. Sodium bicarbonate is absorbed and predisposes to alkalosis and the formation of stones in the kidneys.
4. All the carbonates bring on belching as their carbon dioxide is released by hydrochloric acid.
5. The aluminum salts have an astringent taste and are expensive, and since they appear to exert their best influence in liquid suspension they must be taken in large amounts.

### THE IDEAL ANTACID

The ideal antacid should be palatable, nonabsorbable and capable of neutralizing the gastric acid when taken in relatively small quantities. It should be a solid so that it can be carried about in capsules or envelopes without fear of bottle breakage. It should not remove chloride or phosphate in undue amounts from the digestive tract or otherwise alter mineral metabolism. It should not alkalize the urine and result in the precipitation of calculi. It must not cause either constipation or diarrhea or any irritation of the digestive tract. It must be reasonably priced, as large quantities must be taken over long periods. It should cause no belching and must give no offensive odor to the stool or breath.

### EXPERIMENTS WITH "AMBERLITE IR IV"

In the hope that one of the synthetic plastic resins might approach this ideal as an antacid, Segal [4] at Rochester, N. Y., and Martin [5] in Philadelphia in 1945 began experimental work on the acid-neutralizing qualities of "amberlite IR IV." "Amberlite IR IV" is a resin produced by condensation of diphenylol dimethylmethane and formaldehyde in a basic medium. Both workers agreed that the resin was innocuous for laboratory animals. Rats, 20 per cent of whose diet consisted of resin, showed normal growth and there were no ill effects on any organ when they were killed after eight months.

Martin found that by finely grinding "amberlite IR IV" (metaphylene diamine) in a ball mill its acid-adsorbing quality was enhanced manifold.

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4. Segal, H. L.; Hodge, H.; Watson, J. S., and Scott, W. W. J.: A Polyamine-Formaldehyde Resin, Gastroenterology **4**:484 (June) 1945. Segal, H. L.; Hodge, H. C.; Watson, J. S., and Coates, H.: A Polyamine-Formaldehyde Resin, Gastroenterology **9**:199 (Feb.) 1947.

5. Martin, G. J., and Wilkinson, J.: The Neutralization of Gastric Acidity with Anion Exchange Resins, Gastroenterology **6**:315 (April) 1946.

Martin's 200 mesh resin presented possibilities as a therapeutic agent for peptic ulcers as it had five times the acid-neutralizing power of Segal's larger mesh resin. "Amberlite IR IV" as supplied is a powdery amber substance insoluble in the common solvents and with a faint phenolic odor.

We have made neutralization experiments on the freshly extracted gastric juice of 100 patients. The free acid in these specimens varied from 6 to 69 clinical degrees, and the amounts ranged from 15 to 100 cc. Some of the experiments were performed at room temperature and others at 99 F. Toepfer's reagent was used as an indicator. Martin's resin was added, with constant stirring. It was found that neutralization (though usually immediate) required as much time as forty-five minutes in 1 case. On the average, 50 cc. of gastric juice of 62 degrees of acidity was neutralized immediately by 0.2 Gm. of resin. The viscidity of the juice appears to be a factor in determining the number of resin particles exposed to acid and thus in the rate of neutralization.

We also titrated Martin's resin against twentieth-normal hydrochloric acid to $p_H$ 4 and compared its neutralizing action with that of calcium carbonate and an aluminum hydroxide suspension ("amphojel"). One hundred cubic centimeters of twentieth-normal hydrochloric acid was neutralized by 0.2 Gm. of calcium carbonate, 0.6 Gm. of resin or 38 cc. of "amphojel." These experiments suggested the possibility of using the resin as an acid-neutralizing agent to treat peptic ulcer in amounts somewhat greater than those of calcium carbonate and less than those of "amphojel." Spears [6] arrived at a similar dosage by a different method. Since gastric secretion and $p_H$ varies from time to time and from one person to another it is difficult to estimate dosage for any antacid.

## CLINICAL STUDIES

A preliminary report [7] has been published on the use of resin in the treatment of 36 cases of peptic ulcer. We have now used the preparation in 60 cases for from one to ten months and find that it is just as satisfactory as the usually employed metallic salt antacids and has few of their disadvantages. It causes neither constipation nor diarrhea. Patients have taken from 2 to 9 Gm. of the drug daily for from six to eight months with no evidence of toxicity as manifested by examination of the skin, blood and urine. No damage to the gastric mucosa was noted in 3 patients in whom the stomach was resected and in 3 on whom gastroscopy was performed.

6. Spears, M. M., and Pfeiffer, M. C. J.: Anion Exchange Resin and Peptic Ulcer Pain, Gastroenterology **8**:191 (Feb.) 1947.

7. Kraemer, M., and Lehman, D. J.: The Treatment of Peptic Ulcer with Anion Exchange Resin, Gastroenterology **8**:202 (Feb.) 1947.

At first the resin was given in bulk in teaspoonfuls (3.5 Gm.), but since some of the patients complained of a sandy or powdery feeling of the tongue and throat, capsules containing resin were substituted, each capsule containing 0.25 Gm. The dose was reduced to 0.5 Gm. to 1 Gm. six to ten times daily.

For most of the patients the management was ambulatory, with the diet and antacid schedule as shown in table 2. The hospitalized patients were treated according to the schedule shown in table 1. We have

TABLE 1.—*Hospital Diet and Directions for Treatment of Complicated Peptic Ulcer*

**Standing Orders for Nurses**

**This diet is prescribed for patients who are suffering from acute hemorrhage, partial pyloric obstruction, gastric ulcer and penetrating duodenal ulcers. For the first three days the patient must be kept in bed except when using the toilet. In cases of bleeding ulcer a bedpan must be used. Visitors restricted.**

**Feedings and medication must be given exactly at time ordered**

| | |
|---|---|
| 7:55 a. m. | Atropine sulfate, 0.0003 Gm.; phenobarbital, 0.015 Gm. |
| 8 a. m. | Cooked cereal, 4 oz. (120 Gm.); sugar, 1 drachm (4 Gm.); cream, 1 oz. (30 cc.); milk, 8 oz. (250 cc.) |
| 9 a. m. | Antacid |
| 10 a. m. | Milk, 8 oz. |
| 11 a. m. | Antacid |
| 11:55 a. m. | Atropine sulfate, 0.0003 Gm.; phenobarbital, 0.015 Gm. |
| 12 noon | Puréed vegetables, 4 oz., with butter; mashed potato, 4 oz., with butter; cup custard |
| 1 p. m. | Antacid |
| 2 p. m. | Milk, 8 oz. |
| 3 p. m. | Antacid |
| 4 p. m. | Milk, 8 oz. |
| 4:55 p. m. | Atropine sulfate, 0.0003 Gm.; phenobarbital, 0.015 Gm. |
| 5 p. m. | Puréed vegetables, 4 oz., with butter, mashed potato, 4 oz., with butter; jello and cream, 1 oz. (30 Gm.) |
| 6 p. m. | Antacid |
| 7 p. m. | Milk, 8 oz. |
| 8:30 p. m. | Antacid |
| 10 p. m. | Milk, 8 oz. and antacid; atropine sulfate, 0.0003 Gm.; phenobarbital, 0.09 Gm. |
| 12 | Milk, 8 oz. and antacid |
| 3 a. m. | Milk, 8 oz. and antacid |
| 6 a. m. | Milk, 8 oz. and antacid |

**Ascorbic acid tablet, 100 mg. three times a day by mouth; 1 cc. of vitamin B complex intramuscularly daily**

**After four days of this diet if the patient is symptom free add to diet as follows:**

| | |
|---|---|
| 8 a. m. | Puréed prunes, 4 oz., slice toast, butter and soft-boiled egg |
| 12 noon | Milk soup, 4 oz. (120 cc.), slice toast and butter |

**If the patient has no night pain the feedings after 10 p. m. may be discontinued after the third day**

used these diets for many years. They are convenient and serve as standards for the clinical comparison of antacids. The antispasmodic employed is atropine sulfate and the dose 0.0003 Gm. The first 5 patients in our study were on our "semiambulant" or "hospital" ulcer regimens and used magnesium trisilicate or aluminum phosphate gel as antacids. Then resin was substituted, and they continued to do well except for 1 patient with a gastric ulcer who later also failed to benefit from aluminum hydroxide and on whom it was necessary to perform subtotal gastric resection. The next 55 patients were started on the

diets which included the "amberlite" as the sole antacid. Forty-five of the patients were ambulatory, and 15 were hospitalized. There were 3 patients with severe hemorrhage who also required transfusions. These three responded well to resin therapy.

In general, freedom from pain is evidence of the healing of an ulcer. While a symptomless ulcer is not necessarily an inactive one, the excep-

TABLE 2.—*Ulcer Diet for Semiambulant Patients*

During the period of this diet, which should last several weeks, the patient should rest as much as possible. Relax, avoid arguments and do not see too many visitors. Follow the schedule explicitly. If you must work, go to bed for your evening meal and stay there. Spend most of your time off in bed. Choose from the allowed foods. Eat small meals.

**Schedule**

| | |
|---|---|
| 7:55 a. m. | Antispasmodic |
| 8 a. m. | 1 plate of cooked mashed prunes, passed through a collander, ½ cup of cooked cereal ("cream of wheat," "farina," "hominy," "pablum" or oatmeal), 1 soft-boiled egg, 1 slice of toast and butter, milk or "kaffe hag" or "sanka" with cream |
| 9 a. m. | Antacid |
| 10 a. m. | Glass of milk |
| 11 a. m. | Antacid |
| 11:55 a. m. | Antispasmodic |
| 12 noon | Any milk or creamed soup unseasoned and strained. Cream cheese sandwich. White bread and butter. Purée of peas, lima beans, carrots, asparagus tips, beets, squash, spinach, or cauliflower. ½ cup of steamed or boiled rice, macaroni, spaghetti or noodles with butter, 1 slice of toast and butter. Gelatin preparations of rice, tapioca, bread or custard puddings without raisins or nuts, or stewed fruits if passed through a collander and without syrup |
| 1 p. m. | Antacid |
| 2:30 p. m. | Glass of milk |
| 3:30 p. m. | Antacid |
| 4:30 p. m. | Glass of milk |
| 5:55 p. m. | Antispasmodic |
| 6 p. m. | One soft-boiled egg, or plain omelet or cottage cheese with sweet cream. Puréed vegetable as at luncheon. Small baked potato without skin but with butter. Desserts as at luncheon. Toast and butter |
| 7 p. m. | Antacid |
| 8:30 p. m. | Glass of milk |
| 9:30 p. m. | Antacid |
| 10:25 p. m. | Antispasmodic |
| 10:30 p. m. | Glass of milk and antacid |

Set alarm clock for following hours;* when awakened drink a glass of milk and take the antacid

Do not use seasoning for any of these foods. A pinch of salt may be used
Milk may be malted. You may drink tap water without ice as you wish
If any questions arise, telephone the physician

* Patients with night pain are advised to set alarm so that they awaken a half hour before the onset of pain.

tions to this rule are so infrequent that it may be used for the purpose of evaluating the effect of various antacids.

On this basis 47, or about 80 per cent, of our patients have done well on resin therapy. Six patients did not respond well to resin or to any other antacid therapy and required subtotal gastric resection. Three patients did not respond to resin therapy but did well when given other antacids. Two patients were not relieved by resin or other antacids but were kept free of symptoms by nightly aspirations of gastric contents. Two cases could not be followed adequately.

## COMMENT

While much more research on resins is needed, it is now apparent that they are of value as antacids in the treatment of peptic ulcer. In addition to their neutralizing effects on gastric juice they are known to be effective adsorbers of pepsin. As pepsin is inactivated at a $p_H$ of 4 we are not in a position to know if improvement resulted from a change in $p_H$ or from pepsin adsorbtion. Since "amberlite" is insoluble it is not absorbed from the digestive tract and theoretically is recoverable from the bowel quantitatively as digested. The exact method by which acid is removed from solution is not known. A possible equation follows, in which R signifies resin:

$$R{\cdot}NH_2 + HCl \rightarrow R{\cdot}NH_2{\cdot}HCl$$

In the small bowel, as in any alkaline medium, the adsorbed hydrochloride acid is released as follows:

$$R{\cdot}NH_2{\cdot}HCl + NaHCO_3 \rightarrow R{\cdot}NH_2 + NaCl + H_2CO_3$$

Thus there is no withdrawal of chloride from the digestive tract.

We have found capsules the best form in which to administer the resin. When it is given in powder form, as mentioned, patients complain of a sandy feel on the tongue. When suspended in liquid, it loses some of its acid-adsorbing qualities. Resin will not hold together as a tablet, as there is some inherent elasticity in the molecular particles which causes a compressed tablet to expand and fall apart after a few days. This difficulty should be overcome in time. The cost of the crude drug is so low that it should be marketed at a price which even the poorest can afford.

## SUMMARY

A synthetic plastic resin with acid-adsorbing qualities has been used to treat 60 patients with known peptic ulcer. This resin, "amberlite IR IV," appears to be as effective as the usually employed salts of calcium, magnesium and aluminum but does not produce any of their untoward reactions. It approaches the ideal antacid in that it is not absorbed from the digestive tract, has no effect on the acid-base balance and does not alkalize the urine. It does not affect the bowels or irritate the gastric mucosa. It neutralizes acid rapidly and promptly relieves pain. It is effective in small dosage and is inexpensive and tasteless.

234 Roseville Avenue.

## ABSTRACT OF DISCUSSION

DR. WALTER L. PALMER, Chicago: The secretaries of the two Sections are to be congratulated on the splendid program.

With regard to Dr. Levin's paper showing that in patients with duodenal ulcer the amount of acid secreted is about three and one-half times that in the normal group, the question is still not answered as to whether this hypersecretion is a primary mechanism or whether it is secondary to the ulcer. However, it is clear that gastric and duodenal ulcers and also jejunal ulcers are in fact peptic ulcers

because they occur only when there is adequate peptic activity. We do not know why it is that the mucosa breaks down in certain circumstances or indeed what these circumstances are.

Dr. Pollard's paper on the use of "enterogastrone" was most interesting and further points out the fact that the use of this is still in the experimental stage. I am reminded of the wave of enthusiasm which swept the country a number of years ago for "larostidin". I am sure that we are anxious to avoid another mistake such as that

With regard to the paper by Dr. Kraemer on a new antacid, I must say frankly that I am not persuaded that it is any better than calcium carbonate. If someone would find a way to make money out of calcium carbonate, the retail men would sell it in very large quantities.

Vagotomy combined with gastroenterostomy is a substitute for subtotal gastrectomy for duodenal ulcer and, in my judgment, is greatly to be preferred.

Dr. M. I. Grossman, Chicago: In Chicago we who are associated in the clinics and laboratories with Dr. Ivy are continuing the use of "enterogastrone" in the treatment of peptic ulcer. Our results continue to be favorable.

As is evident from Dr. Pollard's presentation today, "enterogastrone" is not, at the present stage of its development, successful in reducing gastric secretion and its effectiveness in the treatment of peptic ulcer does not depend on this ability.

"Enterogastrone" is not, and we do not claim it to be, more successful in the management of the acute exacerbation of peptic ulcer than is standard medical management.

It is in the prevention of recurrence of peptic ulcer that "enterogastrone" therapy has its special field of usefulness, according to our observations on dogs.

I should like to join Dr. Palmer and Dr. Bockus, who spoke before the American Gastro-Enterological Association several days ago, in emphasizing that at the present stage of development of the use of this material there is going to be a rush of the use of untested and untried materials throughout the country, and now that we have been able to show that this material may have benefit, the greatest emphasis must be placed again on the laboratory approach in standardizing these materials so that they may be properly used in the clinic.

Dr. Mildred C. J. Pfeiffer, Philadelphia: Dr. Spears and I have used the same amberlite or resin as employed by Dr. Kraemer since June 1945, and in the main our findings and those of Dr. Kraemer are similar.

Medically, in uncomplicated peptic ulcers this antacid and pepsin inactivator has certain advantages, but in the complicated case the resin in our hands has had nothing significant to offer as a substitute for surgical intervention.

The surgical indications remained the same, and this was especially true of ulcers which were of the posterior and superior aspects of the duodenum just beyond the pylorus, with or without obstruction, and which were penetrating into the pancreas.

Complete relief of pain with the use of the resin was not synonymous with healing, and the incomplete relief of pain helped to exclude the ulcer from the uncomplicated category.

Dr. Hyman I. Goldstein, Camden, N. J.: Let us have a "moratorium" on further "new" antacids and absorbents and other so-called remedies and procedures for the "modern" treatment of peptic ulcer. Not, as Russell Boles says, for a mere hundred years but for two thousand years has "acidity" been considered a factor in ulcers. Celsus (circa 35-10[?] B. C.) advised patients with ulcer to avoid acid and acrid substances. Diocles (circa 350 B. C.) described the symptoms of ulcer and spoke of "ructus acidus," "vehementes *dolores*" and "flatus" (quoted by

Galen [130-200 A. D.] in his "De locis affectis," Paris, 1513, liber III, cap. vi), and Paul Aegineta (625-690 A. D.), Spigelius, Scultetus, Riolan and many others centuries ago used milk and aluminum silicate, or "kaolin-terra sigellata," in the treatment of peptic ulcer. Usher Parsons (1840) knew of "psychosomatic medicine" and the psychic effect on the digestive apparatus, as did the late Jacob Kaufmann, of New York, decades ago!

The speakers have overlooked the work of Sir Gilbert Blane (1749-1834), naval physician, "on the effect of the pure fixt alkalies and of lime water in several complaints" (*Tr. Soc. for Improvement of Med. and Surg. Knowledge* **2**:138-141, 1800, London) published nearly one hundred and fifty years ago but read on March 1, 1796. Here he discusses the use of alkalis in gastric complaints, mentioning the mild alkalis, magnesia, common calcareous earth, lime water and pure alkalis as having a favorable effect on "gastric acid . . . which may be secreted in so concentrated a state, or in such quantity, as to constitute disease." This was in 1796, twenty-eight years before William Prout discovered hydrochloric acid in the gastric juice.

The program today, with the many "remedies" listed, is proof that we have not advanced very far, and that we must still look to the future for the better control and "cure" of peptic ulcer, the correction, if humanly possible, of the "ulcer constitutional diathesis" and the causation.

Surgery has progressed rapidly, particularly gastrointestinal surgery, since the first successful gastrotomies by Florian Mathis in 1602 and Daniel Schwalbe on July 9, 1635, and the successful resection of 5 feet of intestines in a 13 year old boy by John Nedham (*Philosoph. Trans. 49, part 1, 1755; Obs. 37, 238-239, pub. 1756, London*). The resection was performed (successfully) on Jan. 5, 1755—nearly two hundred years ago. The first successful resection of the stomach (in a dog) was by Daniel C. T. Merrem (1790-1859) in 1810, and pylorectomies were performed by Jules Péan in 1879 and T. Billroth in 1881. How will the surgeons remove the "ulcer diathesis" by vagectomy, "partial vagectomy" or vagal neurectomy (the term "vagotomy" is incorrect)? Why do duodenal ulcers never become malignant and gastric ulcers, all too often, show evidence of malignant change? And why do gastric and duodenal ulcers frequently perforate, whereas gastric cancer rarely perforates?

Dr. David J. Sandweiss, Detroit: Dr. Winkelstein stated that Dr. Levin's results on nocturnal gastric secretion agree with his and disagree with those which my associates and I have previously reported. I wish to call Dr. Winkelstein's attention to the fact that while Dr. Levin's results appear to indicate that patients with duodenal ulcer on the average show a hypersecretion when compared with his normal group the data on normal subjects agree with our data and completely disagree with those reported by Winkelstein. Whereas Dr. Winkelstein reports that normal subjects during the night secrete little or no free hydrochloric acid and that specimens are difficult to obtain in most instances because of the small amount of night secretion, Dr. Levin has shown that normal subjects secrete on the average of 640 cc. of gastric juice during the twelve hour period of the night, with an average hydrochloric acid concentration of 29 clinical units (range, 1 to 90). It is important to point out that Dr. Winkelstein's studies consisted only of intermittent aspirations (not continuous suction). We found also that with intermittent aspirations patients with ulcer secrete a higher volume of gastric juice than normal subjects, which we interpreted as being due to delayed emptying rather than to hypersecretion. I might also call Dr. Winkelstein's attention to the fact that secretions of 20 per cent of Dr. Levin's patients with ulcer were within normal ranges.

Our own studies on night secretion were concerned with ambulatory patients who had no distress or had it only to a mild degree. All Dr. Levin's patients, however, were patients who were admitted to the hospital because of pronounced distress. None of our patients had retention; 19 per cent of Dr. Levin's patients had retention. Dr. Levin's normal subjects were allowed to eat whatever they desired up to 12:30 p. m. on the day of the study, and his patients with ulcer were given a clear, liquid diet throughout the period of investigation. Our patients with ulcer were kept on a regimen similar to that for our normal subjects. Dr. Levin's test meal (at 5:30 p. m.) consisted of 6 Gm. of protein, 37 Gm. of carbohydrates and no fat. This test meal is different from the one which we employed, which consisted of a fairly well balanced average meal, with 45 Gm. of protein, 110 Gm. of fat and 43 Gm. of carbohydrate. We started our continuous suction six hours after the test meal (at midnight) and conducted continuous aspiration for seven hours thereafter. Dr. Levin began his aspirations only three hours after the meal (at 8:30 p. m.) and conducted continuous aspiration for twelve hours. Our studies took into consideration the entire intestinal phase of gastric secretion, whereas Dr. Levin's studies did not. These differences in the experimental designs might well explain the differences in our results. It is essential that workers in this field agree on a standard experimental procedure, especially if the data are to be interpreted on a comparative basis as was attempted by Dr. Winkelstein.

With respect to enterogastrone, I should like to state that on the basis of our experience to date enterogastrone offers very little if anything of therapeutic value to patients with ulcer. It is our opinion that the use of enterogastrone is still in the experimntal state. The physiologic and biochemical elements of this preparation need further intensive study.

Dr. A. F. R. Andresen, Brooklyn: Can anyone say that we know the causation and pathogenesis of ulcer? If we did know that, we would long ago have found a cure. There would not be any need for such discussions as we have had this afternoon. There is only one thing which is known about peptic ulcer, and that is that the uncomplicated peptic ulcer heals spontaneously and rapidly and often in spite of treatment. It is known that without treatment a good many ulcers will heal within two or three weeks. We know that because of the frequent history of the rapid disappearance of symptoms in previous attacks, without treatment. We know it because during the intervals between attacks no roentgenologic evidence of ulcer is present. We know it from the finding at autopsy of many scars of healed ulcers, and we know it from the work of Lewis Gregory Cole, who showed us how the rapid healing of an ulcer can be demonstrated by roentgenologic studies.

During this spontaneous healing of an ulcer there is always present a considerable amount of acid, so that it is just as logical to conclude that the acid is a part of the protective reaction of the stomach against the presence of an ulcer as it is to consider that it is the cause of ulcer. There is no evidence at all that ulcer is caused by acid. We know that normal mucosa is not digested by pepsin-hydrochloric acid. An area of mucosa must be dead before it can be digested and an ulcer produced. The end artery supplying the area must be blocked in some way by embolism, thrombosis and, some think, spasm, but the reason for the blockage has not been conclusively demonstrated. Perhaps some histamine-like substance in the blood may account for it. I submit the thought that perhaps the healing of the ulcer is promoted by the cleaning out of the debris from the base of the ulcer by this protective acid secretion.

Surgeons tell us that they operate for complications of ulcer, yet the main discussion which we hear on the part of surgeons is about the effect that operation

has on the ulcer. When they discuss what effect it has on the ulcer they are going far afield, because we know that the simple ulcer will heal in spite of anything that is done. In complicated ulcer an operation is required for the complication and not for the ulcer itself. None of the operations so far devised will prevent recurrence.

Dr. Manfred Kraemer, Newark, N. J.: I should like to reply to Dr. Pfeiffer and Dr. Palmer. I want to thank Dr. Pfeiffer. I am not in complete accord with her suggestion that the absence of pain is not evidence of healing of ulcer. It usually is, and for clinical purposes absence of pain means healing.

In regard to what Dr. Palmer said, I think that in Chicago there must be a lot of persons with irritable colons because his patients there have no complaints on use of calcium carbonate. In New Jersey, where most of the patients with ulcer have normal bowels, calcium carbonate has a constipating effect. We are looking for an improvement on calcium carbonate, for which there is a definite need.

# PSEUDOTUMOR OF BONE IN HEREDITARY PSEUDOHEMOPHILIA

HOWARD S. J. WALKER, M.D.
AND
NATHAN A. WOMACK, M.D.
ST. LOUIS

PATIENTS with prolonged bleeding time either from true hemophilia or from so-called pseudohemophilia commonly present symptoms referable to hemorrhage into major joints. Hemorrhage into bone itself is much less common, and frequently the resulting lesion is difficult to differentiate from some form of bone tumor. Such a situation was recently encountered in a case of pseudohemophilia.

## REPORT OF A CASE

G. L. H., a 33 year old white married man of German extraction, entered Barnes Hospital on Dec. 16, 1946, with the complaint of swelling of his right thigh for sixteen years. He had always bled freely after relatively minor injuries but appeared to bleed more on some occasions than on others. At times he did not bleed any more than would be normal for the trauma incurred. At one time in his childhood he bled for two weeks after a minor cut on the tongue. He had had frequent moderately severe epistaxes for many years, but these ceased without treatment. Otherwise, his general health had been marred only by frequent colds and sore throat.

His father and his maternal grandfather both suffered from frequent nosebleeds on slight provocation. These sometimes lasted for many hours before ceasing spontaneously. The genealogic chart is presented for more detailed information (fig. 1).

His present illness began after a minor injury in a basketball game in 1930. A hard "knot" developed on the medial aspect of the lower end of the right thigh. At this time he was 16 years of age. This remained asymptomatic until three years later, when his leg "gave way while running" and examination showed what apparently was a pathologic fracture. A long thigh cast was applied for many months, and he began weight bearing about one year after injury. The thigh and knee remained greatly swollen after this fracture, and there was practically no motion in the knee joint. During the next few years the right leg became 3 to 4 inches (7.6 to 10 cm.) shorter than the left, which was due presumably to failure of longitudinal growth. Since 1940 he had been unable to walk without crutches because of instability of the thigh. It would bend above the knee and feel as though it would give way when any stress was placed on it.

On Aug. 5, 1943, he first entered the Barnes Hospital. Physical examination at that time revealed that the lower part of the right thigh and the knee were

From the Department of Surgery, Washington University School of Medicine, and Barnes Hospital.

greatly enlarged. There was some increase in firmness of the swollen areas, and the knee joint was fixed, but the patient experienced little tenderness and discomfort.

Because of the history of bleeding he was given hematologic examination (Dr. C. V. Moore), but no definite diagnosis of hemophilia could be made, since all the laboratory findings were considered to be normal. His condition was diagnosed as an atypical familial hemorrhagic diathesis, and this may be catalogued under the broad term pseudohemophilia. Laboratory findings were as follows: The red blood cell count was 5,160,000, the white blood cell count 5,650, the platelets 949,440, the hemoglobin content 15.8 Gm. and the reticulocytes 4.2 per cent. The differential count revealed no basophils, 1 per cent eosinophils, no myelocytes or juvenile cells, 5 per cent stab forms, 56 per cent segmented cells, 29 per cent lymphocytes and 9 per cent monocytes. There was slight anisocytosis. Bleeding time was four minutes, prothrombin time was normal and clotting time

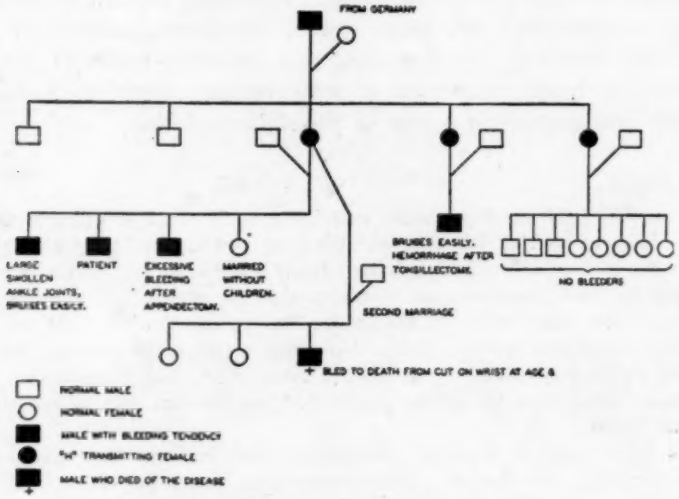


Fig. 1.—Genealogic chart.

was twenty-five minutes. Examination of the urine revealed a specific gravity of 1.018, a $p_H$ of 7.0 and no albumin or sugar. Microscopic examination revealed nothing abnormal.

Roentgenologic examination revealed a lesion of the lower end of the right femur resembling a giant cell tumor. Because of his bleeding tendencies, the patient was treated with high voltage roentgen rays, and he was discharged on Aug. 15, 1943.

This treatment provoked an erythema, followed by desquamation and pigmentation of the epidermis, but it was otherwise fruitless. His condition remained relatively stationary until November 1946, when he noted a sudden onset of moderately severe, throbbing pain in the tumor just above the knee. This was followed in seven to ten days by a rapid increase in the size of the entire thigh, with exacerbation of the pain and discoloration of the skin. A few days after this appeared he began to have intermittent attacks of nausea and vomiting. On a few occasions he had severe burning pain in the region of the esophagus and vomited some coffee ground material. No tarry stools were noted.

He reentered Barnes Hospital on Dec. 16, 1946. At this time the right lower extremity was found to be tense, ecchymotic, tender and hot. It was tremendously and almost cylindrically enlarged from the groin to below the knee. The knee was immobile, but a false joint was present 10 to 15 cm. above it. This allowed only slight motion.

Laboratory findings at this time revealed a red blood cell count of 3,750,000, a white blood cell count of 12,000, a hemoglobin content of 8.6 Gm. and a platelet count of 366,000. The differential count showed 2 per cent basophils, 1 per cent eosinophils, 6 per cent myelocytes, 3 per cent juvenile cells, 5 per cent stab forms, 50 per cent segmented cells, 18 per cent lymphocytes and 15 per cent monocytes. The hemoblasts numbered 2 for every hundred red blood cells. Examination of the urine revealed a specific gravity of 1.015, a $p_H$ of 6.0, no albumin or sugar and no microscopic abnormalities. The nonprotein nitrogen was 13 mg. per hundred cubic centimeters. Reaction to the Kahn test of the blood was negative.

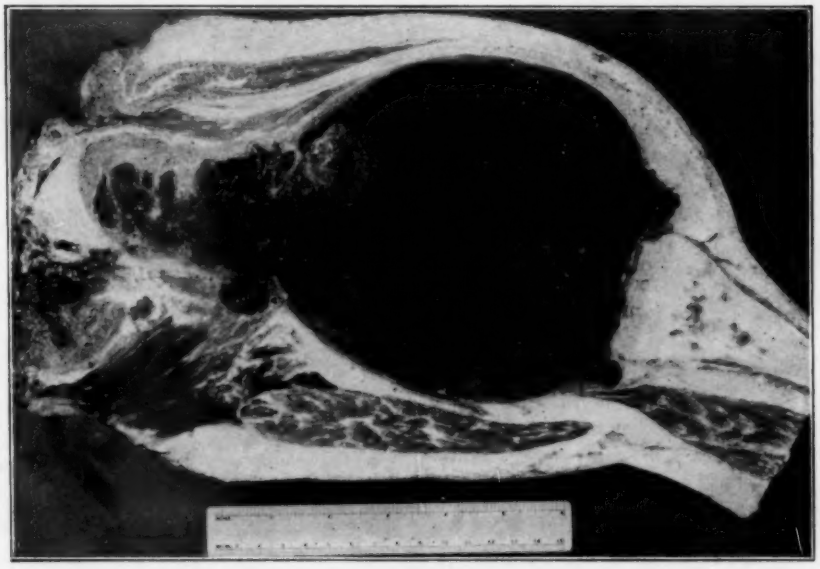

Fig. 2.—Sagittal section of thigh after amputation. There is considerable shortening due to destruction of the femur.

The sugar content was 97 mg. per hundred cubic centimeters. Total protein was 5.1 Gm. per hundred cubic centimeters, of which 3.0 Gm. was albumin and 2.1 Gm. globulin. Bleeding time was four minutes and clotting time twelve minutes eleven seconds. The cephalin flocculation test gave a negative reaction. The serum calcium was 8.4 mg. and the serum phosphorus 4.8 mg. per hundred cubic centimeters, and the serum phosphatase was 4 Bodansky units. The serum bilirubin (van den Bergh) was 0.23 mg. per hundred cubic centimeters for the prompt direct reaction and 0.34 mg. for the direct reaction. The total bilirubin was 1.01 mg per hundred cubic centimeters (indirect reaction, 0.67 mg.).

Roentgenograms taken at this entry showed a larger defect of the femur, which was again diagnosed as a giant cell tumor. The patient had been confined to his bed for the previous two months. His pain was intense.

In view of the progressive deterioration of his condition, amputation at the hip joint seemed desirable in spite of the danger.

Thirty-six hours before amputation whole blood was administered, and this was continued almost constantly until the day after his operation, a total of 4,500 cc. being given. The thigh was amputated through the lesser trochanter, hemorrhage being controlled by preliminary ligation of the common femoral artery and vein. The muscles of the thigh, particularly the adductors, were damaged by a huge mass of old blood that had extended upward onto the abdominal wall. Although studies of the clotting mechanism preoperatively had shown it to be within normal limits, at no time during the operation was clotting observed. It was necessary therefore to pack the marrow cavity with oxidized cellulose and to ligate each small bleeding point meticulously.

He was given sulfadiazine and penicillin postoperatively. On the first postoperative day he became nauseated and vomited. On the second postoperative day fever began, but there was no obvious infection of the wound. The temperature rose gradually to a maximum of 40.6 C. (105 F.) on the ninth postoperative day but subsided completely on the twelfth day.

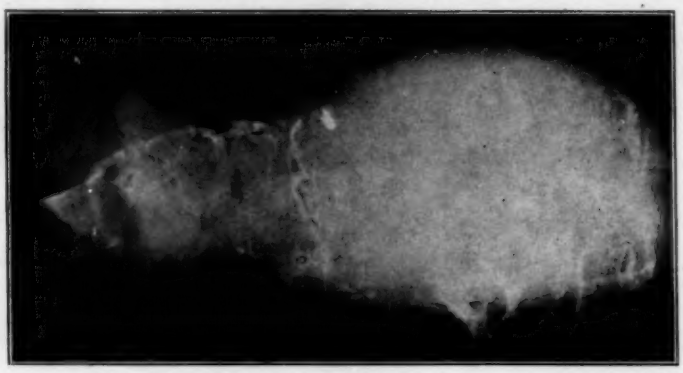

Fig. 3.—Roentgenogram of specimen shown in figure 2.

The use of sulfadiazine was discontinued on the fourth postoperative day. The dose of penicillin was increased on the fifth postoperative day, and administration was discontinued on the sixteenth day.

A small hematoma was evacuated on the sixth postoperative day, and a considerable slough of skin, subcutaneous tissue and muscle occurred on the thirteenth day. The wound granulated well after this.

The patient received 500 cc. of blood on the first, third, fourth and thirteenth postoperative days.

The last blood count, on the twenty-third postoperative day, showed 3,930,000 red blood cells, 5,200 white blood cells, and a hemoglobin content of 13 Gm., with 2 per cent stab forms, 68 per cent segmented forms, 27 per cent lymphocytes and 3 per cent monocytes.

*Pathologic Examination.*—Gross Study: The specimen consisted of almost the entire right lower extremity. The thigh to below the knee was greatly swollen, tense, ecchymotic and nearly cylindric in shape. The leg and foot were normal. The specimen was cut in a sagittal plane. No normal femur was present, the entire lower portion being completely replaced by an ovoid, bright red, clotted mass which measured approximately 15 by 20 cm. and extended out into the

muscles, which it seemed to destroy by pressure. The joint space was not involved. Slender trabeculae of bone were all that remained of the lower part of femur. Sections were taken from all areas for microscopic study.

Microscopic Study: Sections taken from the center of the mass showed only blood and some connective tissue. Farther out degenerated skeletal muscle heavily infiltrated with blood could be seen. Some areas contained bone which was necrotic and being absorbed. In other areas osteoid tissue was present, replacing living bone. Numerous areas of giant cell reaction were seen. Abnormal cartilage formation and spicules of new bone were frequent.

Fig. 4.—Dense fibrous osteoid formation adjacent to eburnated bone.

There was no evidence grossly or microscopically of tumor. The final diagnosis was pseudotumor of bone due to pseudohemophilia.

## COMMENT

There is considerable unanimity of opinion on the definition and diagnosis of many of the blood diseases in which prolonged bleeding is present, but with regard to others different authorities do not agree. The following definition seems to be adequate. "Hemophilia is a constitutional anomaly which depends on the hereditary transmission of a sex-linked, recessive, mendelian characteristic and is characterized by a life long tendency to prolonged hemorrhage and a markedly delayed coagulation time." The disease is transmitted by the female but manifested only in the male.

Pseudohemophilia is a poorly defined term which is used for those cases of familial bleeding which cannot be classified under true hemophilia, multiple hereditary telangiectasia or purpura hemorrhagica. The following rare conditions may then be grouped under the main title of pseudohemophilia.

1. Hereditary hemorrhagic diathesis. A number of cases have been described. They have in common a prolonged bleeding time and a normal coagulation time, but some hematologists believe that the conditions are independent entities.

Fig. 5.—Fibrous tissue between damaged muscle and old hemorrhage, showing complete absence of bone. Note giant cell reaction in lower right corner.

2. Congenital or constitutional afibrinogenemia. This is a definite entity characterized by complete absence of fibrinogen and therefore by complete incoagulability. Strangely enough, bleeding is not always prolonged, though most patients die of hemorrhage eventually.

3. Congenital hypofibrinogenemia. This is a vague symptom complex, with tendency to bleeding, moderate thrombopenia and normal bleeding and coagulation times.

4. Idiopathic hypoprothrombinemia. This is a symptom complex of reduced prothrombin time and occasionally prolonged coagulation time.

5. Others which have not been grouped elsewhere.

The changes in the joints in hemophilia are among the most characteristic manifestations of the disease, and hemophilic arthritis may be satisfactorily divided into the following stages:

A. Acute stage. This occurs when there is extravasation of blood into the joint cavity, the epiphysis or the diaphysis of a bone. The blood in the tissues causes a swollen, tender, hot, reddened joint which is voluntarily immobilized in a position of flexion. The patient may have a temperature of 39 to 40 C. (102 to 104 F.), with a leukocytosis of moderate intensity. The roentgenogram shows only a distended joint cavity in which the fluid is somewhat more radiopaque than that

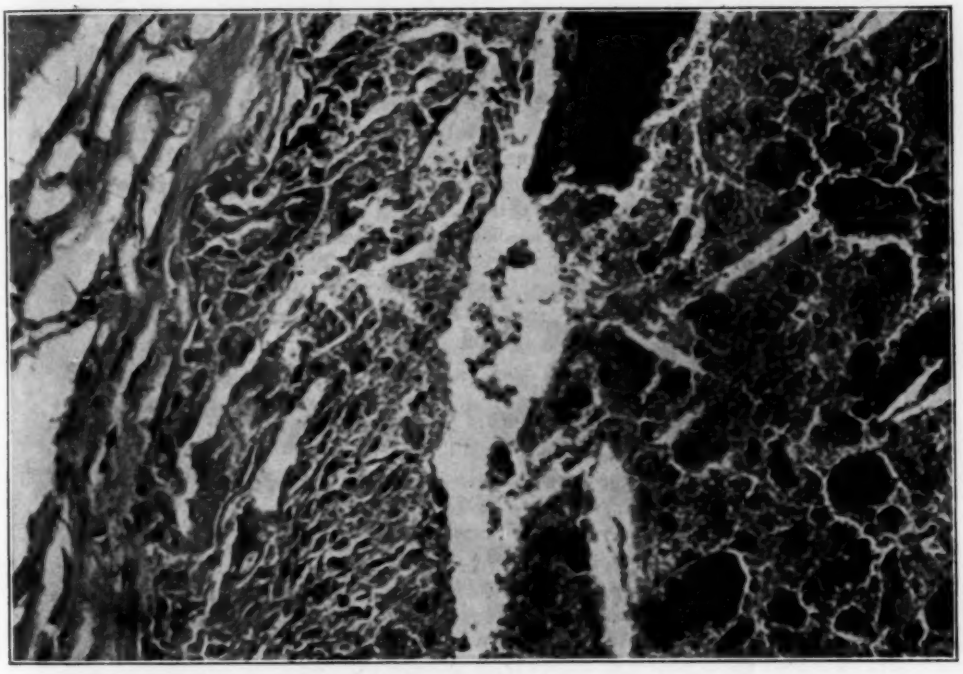

Fig. 6.—Cellular reaction around relatively recent hemorrhage.

in acute synovitis. At this stage the condition may be readily mistaken for an acute pyogenic or traumatic arthritis, and competent surgeons have unwittingly opened such joints.

B. Chronic stage. This is brought about by incomplete absorption of the blood in or about the joints, with resultant permanent changes ranging in severity from minimal thickening of the joint capsule to complete fibrous and bony ankylosis of the joint. Permanent changes are usually brought about only after repeated acute episodes, but most patients have notable deformities by the time they are young adults.

These hemorrhagic and fibrotic changes are widely known, but the osseous changes producing pseudotumors are extremely rare. Accord-

ingly, 4 cases found in the literature, 2 in the American and 2 in the foreign, will be briefly summarized.

CASE 1. (Reported by Firor and Woodhall [1]).—The patient was a 16 year old white boy of Spanish extraction who was known to have hemophilia when he was first seen. He presented a tumor of the right thumb, which had appeared after slight trauma. This was extremely painful, and the radiologic impression was sarcoma of the bone. The thumb was amputated, and bleeding was successfully controlled with the electrocautery. Convalescence was uneventful. Pathologic study proved that the lesion was hemorrhage with pressure necrosis of the metacarpal bone and the two phalanges, uncomplicated by any neoplastic changes.

CASE 2 (Reported by Echternacht [2]).—The patient was a 13 year old boy with known hemophilia who presented a tumor which partially destroyed the upper end of the left tibia. This had started with a minor injury to the upper third of the shin. It had enlarged gradually for nine weeks and rapidly for three weeks. The roentgenologic diagnosis was (1) old hemarthrosis and (2) sarcoma of the tibia. After an unsuccessful attempt to make a diagnosis by biopsy, a disarticulation at the knee was done with the electrocautery. The patient's course was downhill after this, and he died on the third postoperative day. Pathologic examination revealed the tumor to consist of deep red, jelly-like blood clot, with erosion of the anterior cortex deep into cancellous bone and considerable proliferation of the periosteum. No neoplasm was found.

CASE 3 (Reported by Starker [3]).—The patient was a 14 year old white boy who was known to have hemophilia. He presented himself because of a painful tumor the size of his head on the right thigh. This had been present for eight months, but no history of trauma was given. The roentgenologic diagnosis was hemophilia and sarcoma of bone. The tumor was aspirated, and 750 cc. of pure blood was obtained. The patient died fourteen days later, and at autopsy an encapsulated hematoma was found. This had eroded through the cortex of the femur and into the cancellous bone. The periosteum was thickened and ossified at the superior border of the hematoma, and calcified spicules of connective tissue were seen traversing much of the eroded area. No neoplasm was found. Death was presumably not due to the tumor or to aspiration.

CASE 4 (Reported by Reinecke and Wohwill [4]).—The patient was a 27 year old white man who was known to have hemophilia. He presented himself because of swelling of the thigh of many weeks' duration. There was no history of trauma. The tumor was aspirated, but only blood was obtained under high pressure. Three months later the patient died suddenly of a generalized infection unrelated to the aspiration. At autopsy a large subperiosteal hematoma was found completely surrounding the femur for a distance of 10 cm. There was some erosion of the cortex beneath the hematoma. The periosteum above and below the mass of blood showed thickening and formation of new bone. Granulation tissue, sequestra and some giant cells were seen microscopically, but there was no evidence of neoplasm.

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1. Firor, W. M., and Woodhall, B.: Hemophilic Pseudo-Tumor: Diagnosis, Pathology and Surgical Treatment of Hemophilic Lesions in the Smaller Bones and Joints, Bull. Johns Hopkins Hosp. **59**:237-250, 1936.

2. Echternact, A. P.: Pseudotumor of Bone in Hemophilia, Radiology **41**:565-572, 1943.

3. Starker, L.: Knockenusus durch ein hemophiles, subperiostales hamatom, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **31**:381, 1919.

4. Reinecke, and Wohwill, F.: Ueber hämophile Gelenkerkrankung, Arch. f. klin. Chir. **154**:425-479, 1929.

Our case seems to be unique in the sense that we can find no report in the literature of such bone manifestations having been observed in a patient with so-called pseudohemophilia. The patient presented a problem not only in treatment but in diagnosis as well.

The resemblance to solitary giant cell tumor of bone is significant. The fact that hemorrhage into bone in the presence of a lowered serum calcium level can produce such findings is of great interest in the consideration of the cause of giant cell tumor. The mechanism of the production of such a lesion as we have reported is of interest.

Larson [5] has shown that the intramedullary pressure in normal dogs was approximately one-third the systolic blood pressure. He was able to cause massive necrosis of bone by the maintenance of 180 cm. of water pressure continuously over a period of twelve hours. The effect of this intramedullary pressure was not dependent on the periosteum, as the latter was stripped from a considerable portion of the involved bone. In all his dogs infection eventually complicated the original aseptic necrosis, but this may well have found entry through the apparatus.

These experiments seem to offer an adequate explanation for the production of the lesion reported by us. Originally there was probably intermittent intramedullary hemorrhage, with an increase in pressure followed by necrosis of portions of the femur. In addition there may have been some bone infarcts brought about by organizing clots or emboli. As the necrosis was proceeding, sequestration, absorption and replacement of bone were making considerable architectural changes. The original fracture may have followed such a weakening process, or it may have been caused by a normal amount of trauma. The history on this particular point is not completely clear. However, it is obvious that the presence of a fracture could enhance this process, with the final production of a large lesion, as occurred here.

There are no similar cases reported in the literature. A few cases of osteomyelitis from intramedullary transfusions have been reported, and undoubtedly more have occurred, but these seem to be caused by the introduction of bacteria rather than by aseptic necrosis.

## SUMMARY

1. Hemophilia and pseudohemophilia are defined.

2. The pathologic changes in hemophilia are outlined.

3. Four cases of pseudotumor in hemophilia are reviewed briefly.

4. One case of pseudotumor in pseudohemophilia is presented in detail.

5. A brief discussion of the mode of production of this lesion is given.

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5. Larson, R. M.: Diaphyseal Bone Necrosis, Ann. Surg. **108**:127-140, 1938.

# IS CHRONIC CYSTIC MASTITIS A PRECANCEROUS LESION?

## Ten Year Follow-Up Study of Twenty-Six Cases

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BROOKLYN

CHRONIC cystic mastitis has been known as a clinical and pathologic entity for more than one hundred years (Sir Ashley Cooper, 1831). However, the surgeon consulting the literature is confronted with a multitude of conflicting opinions on the nature of this disease and with contradictory advice as to the proper treatment.

The opinion of Klose and Sebening,[1] Semb,[2] Ewing,[3] Crile and Graham[4] and Cheatle and Cutler[5] that chronic cystic mastitis is a precancerous lesion and that mastectomy is indicated is opposed by authorities like Bloodgood,[6] Campbell,[7] Lewis and Geschickter,[8] Bell and others, who have stated the belief that patients with chronic cystic mastitis are no more liable to the development of cancer of the breast than are those without it. There are still others who contend that while chronic cystic mastitis may predispose to cancer of the breast the incidence of the development of malignant tumors after local removal of chronic cystic mastitis is so low (less than 5 per cent) that mastectomy is not justified as a prophylactic measure (Clagett, Plimpton and Root,[9]

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From the Department of Pathology, St. Francis Hospital, and the Sedgwick County Tumor Clinic, Wichita, Kan.

1. Klose, H., and Sebening, W., in Kirschner, M., and Nordmann, O.: Die Chirurgie, Berlin, Urban & Schwarzenberg, 1929, vol. 3, p. 121.

2. Semb, C.: Fibroadenomatosis Cystica Mammae, Acta chir. Scandinav., 1938, supp. 64, p. 10.

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4. Crile, G., and Graham, A.: Benign and Malignant Tumors of Breast, S. Clin. North America **15**:783-821 (Aug.) 1935.

5. Cheatle, G. L., and Cutler, M.: Tumors of the Breast: Their Pathology, Symptoms, Diagnosis and Treatment, London, J. B. Lippincott Company, 1931, pp. 92-133.

6. Bloodgood, J. C.: Chronic Cystic Mastitis of the Diffuse, Non-Encapsulated, Cystic Adenomatous Type (Shotty Breast), Ann. Surg. **90**:886-903 (Nov.) 1929.

7. Campbell, O.: Relationship Between Cystic Disease of the Breast and Carcinoma, Arch. Surg. **28**:101-156 (June) 1934.

8. Lewis, D., and Geschickter, C. F.: The Relation of Chronic Cystic Mastitis to Carcinoma of the Breast, Surg., Gynec. & Obst. **66**:300-307 (Feb.) 1938.

Warren,[10] Whittmore [11]). They advised local operation, with careful postoperative observation. Boyd [12] accepted this conservative treatment for the management of younger patients but recommended mastectomy for patients over 50 years of age.

Since 1925, many cases of chronic cystic mastitis have been studied in the laboratory of St. Francis Hospital from the clinical and histologic standpoint. In a paper [13] published in 1930, 63 cases were analyzed and the following conclusions were reached. Three types of chronic cystic mastitis can be distinguished histologically: (1) simple chronic cystic mastitis, (2) chronic cystic mastitis with papillary proliferation and (3) chronic cystic mastitis with atypia. There is no relation between the first type of chronic cystic mastitis and cancer of the breast, and local excision of the involved mammary tissue is an adequate treatment. The second type, characterized by papillary proliferation, indicates a neoplastic response to the unknown causative factor, endocrine or chemical, of chronic cystic mastitis. Local removal of the mass is recommended, and postoperative observation at regular intervals is insisted on for at least five years. The third type, chronic cystic mastitis with atypia, is considered a precancerous lesion, and mastectomy without removal of the axillary lymph nodes seems indicated.

A similar belief has been propagated recently by Foote and Stewart,[14] who reviewed the material of the New York Memorial Hospital. These authors concluded that chronic cystic mastitis plays a role in the development of cancer of the breast only as far as papillary hyperplasia is concerned. The latter in some persons becomes, for reasons unknown, cytologically atypical. For the great majority of cases of chronic cystic mastitis Foote and Stewart also recommended conservative measures.

## MATERIAL AND FOLLOW-UP STUDY

Of a recent series of one hundred consecutive specimens of the breast submitted to the laboratory, almost one-half (47) were diagnosed micro-

9. Clagett, O. T.; Plimpton, N. C., and Root, O. T.: Lesions of the Breast: The Relationship of Benign Lesions to Carcinoma, Surgery **15**:413-419 (March) 1944.

10. Warren, S.: The Relation of Chronic Mastitis to Carcinoma of the Breast, Surg., Gynec. & Obst. **71**:257-273 (Sept.) 1940.

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13. Hellwig, C. A.: Surgical Indication in Chronic Cystic Mastitis, Arch. f. klin. Chir. **159**:763-784, 1930.

14. Foote, F. W., and Stewart, F. W.: Comparative Studies of Cancerous Versus Non-cancerous Breasts, Ann. Surg. **121**:6-53 (Jan.); 197-222 (Feb.) 1945.

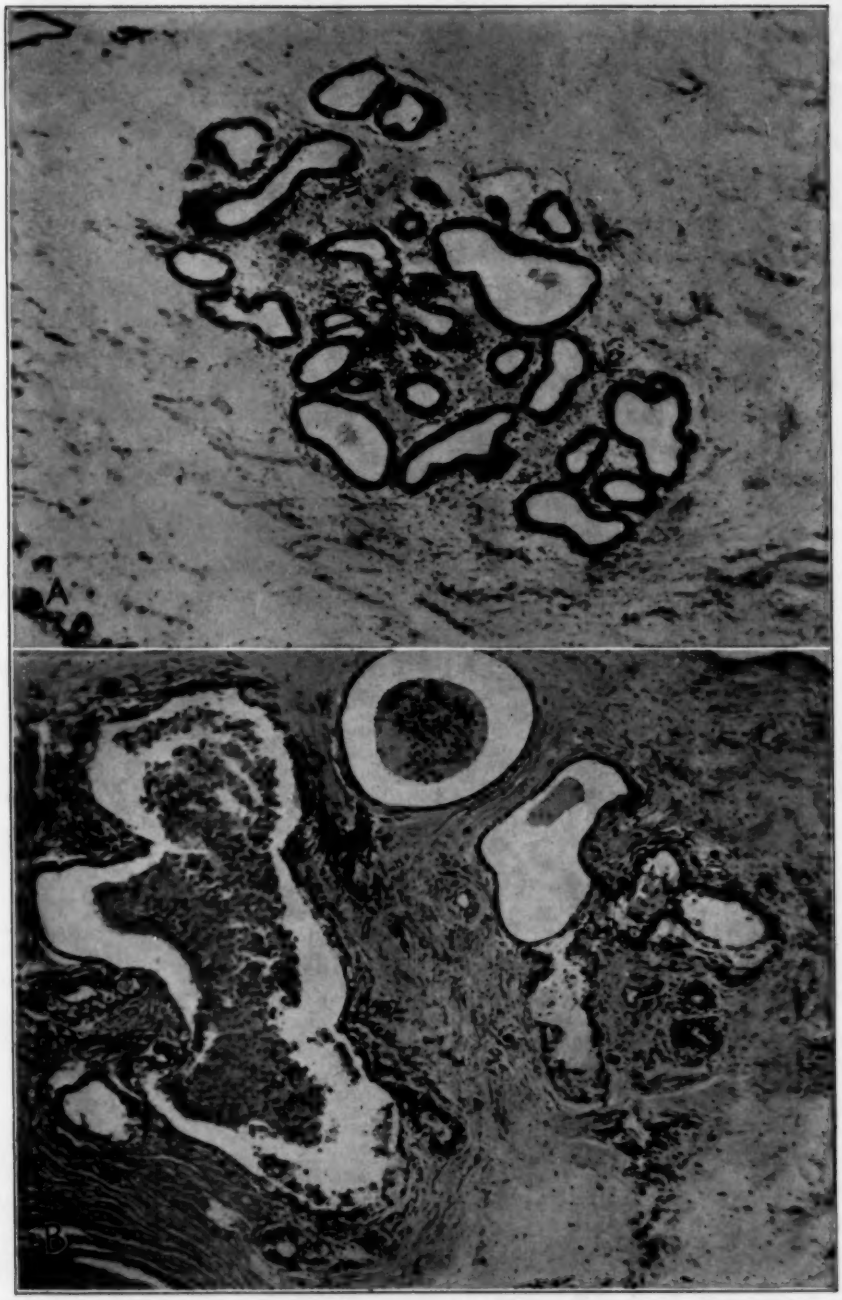

Fig. 1.—*A*, simple chronic cystic mastitis (case 4). Dilated ducts are separated by cellular connective tissue. *B*, simple chronic cystic mastitis (case 7). Wide ducts are filled with lipid-laden histiocytes.

scopically as indicating the presence of chronic cystic mastitis, making it the most common of surgical lesions of the breast. Eight showed atypical epithelial proliferation, and 2 showed papillary hyperplasias. In 3 instances the diagnosis of fibroadenoma was made, and 1 patient complained of bleeding from the nipple.

Twenty-six patients with chronic cystic mastitis who were operated on prior to 1931 were selected for the follow-up study which forms the basis of this paper. The gross specimens and the microscopic slides were reviewed, and the operative procedures and the results of the follow-up studies are recorded in the accompanying table.

*Follow-Up Study of Twenty-Six Cases*

| Case | Age, Yr. | Type of Operation | Histologic Diagnosis | Years of Follow-Up Study | Result |
|---|---|---|---|---|---|
| 1 | 29 | Excision | Simple chronic cystic mastitis | 17 | 2 recurrences, well now |
| 2 | 41 | Excision | Simple chronic cystic mastitis | 15 | Well |
| 3 | 37 | Excision | Simple chronic cystic mastitis | 15 | Well |
| 4 | 35 | Excision | Simple chronic cystic mastitis | 14 | Well |
| 5 | 32 | Excision | Simple chronic cystic mastitis | 14 | Well |
| 6 | 29 | Excision | Simple chronic cystic mastitis | 14 | Well |
| 7 | 42 | Excision | Simple chronic cystic mastitis | 14 | Well |
| 8 | 49 | Excision | Simple chronic cystic mastitis | 14 | Well |
| 9 | 43 | Excision | Simple chronic cystic mastitis | 13 | Well |
| 10 | 44 | Excision | Simple chronic cystic mastitis | 13 | Well |
| 11 | 20 | Excision | Simple chronic cystic mestitis | 13 | Well |
| 12 | 48 | Excision | Simple chronic cystic mastitis | 12 | Well |
| 13 | 39 | Excision | Simple chronic cystic mastitis | 12 | Well |
| 14 | 42 | Excision | Simple chronic cystic mastitis | 11 | Well |
| 15 | 25 | Excision | Simple chronic cystic mastitis | 11 | Well |
| 16 | 34 | Excision | Simple chronic cystic mastitis | 11 | Well |
| 17 | 21 | Excision | Simple chronic cystic mastitis | 11 | Died of pneumonia |
| 18 | 42 | Excision | Simple chronic cystic mastitis | 11 | Well |
| 19 | 27 | Excision | Simple chronic cystic mastitis | 10 | Well |
| 20 | 30 | Excision | Simple chronic cystic mastitis | 10 | Well |
| 21 | 46 | Excision | Papillary proliferation | 14 | Well |
| 22 | 45 | Excision | Papillary proliferation | 11 | Well |
| 23 | 35 | Mastectomy | Atypia | 14 | Well |
| 24 | 40 | Excision | Atypia | 11 | Well |
| 25 | 45 | Mastectomy | Atypia | 11 | Well |
| 26 | 40 | Mastectomy | Atypia | 10 | Died of carcinoma of cervix |

The age of the patients varied from 20 to 49 years, the average being 36 years. Twenty patients had simple chronic cystic mastitis, 2 had papillary proliferation and 4 had atypia. On 23 patients local excision of the involved area was performed, while 3 were subjected to simple mastectomy. The patients were followed for from ten to seventeen years after operation, and all were recently examined by myself or by the attending physician. The results of this survey are as follows: One patient died of cancer of the cervix ten years after, and another of pneumonia eleven years after the operation on the breast. In neither had there been recurrence of chronic cystic mastitis or development of cancer in the breast prior to death. One patient had two local recur-

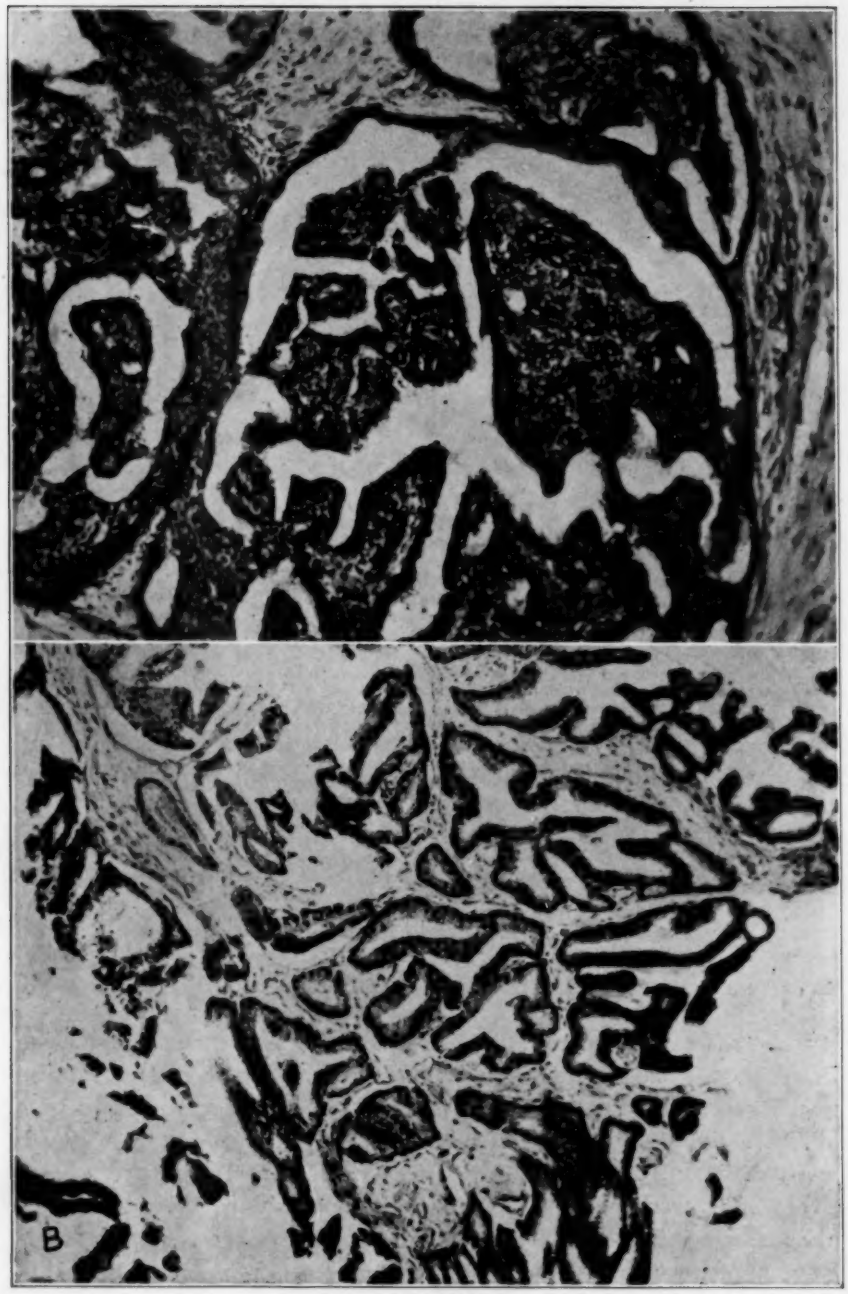


Fig. 2.—*A*, papillary proliferation in dilated ducts (case 21). Local excision has been followed by fourteen years of well-being. *B*, papillary proliferation in duct (case 22). After local excision there was no recurrence for eleven years.

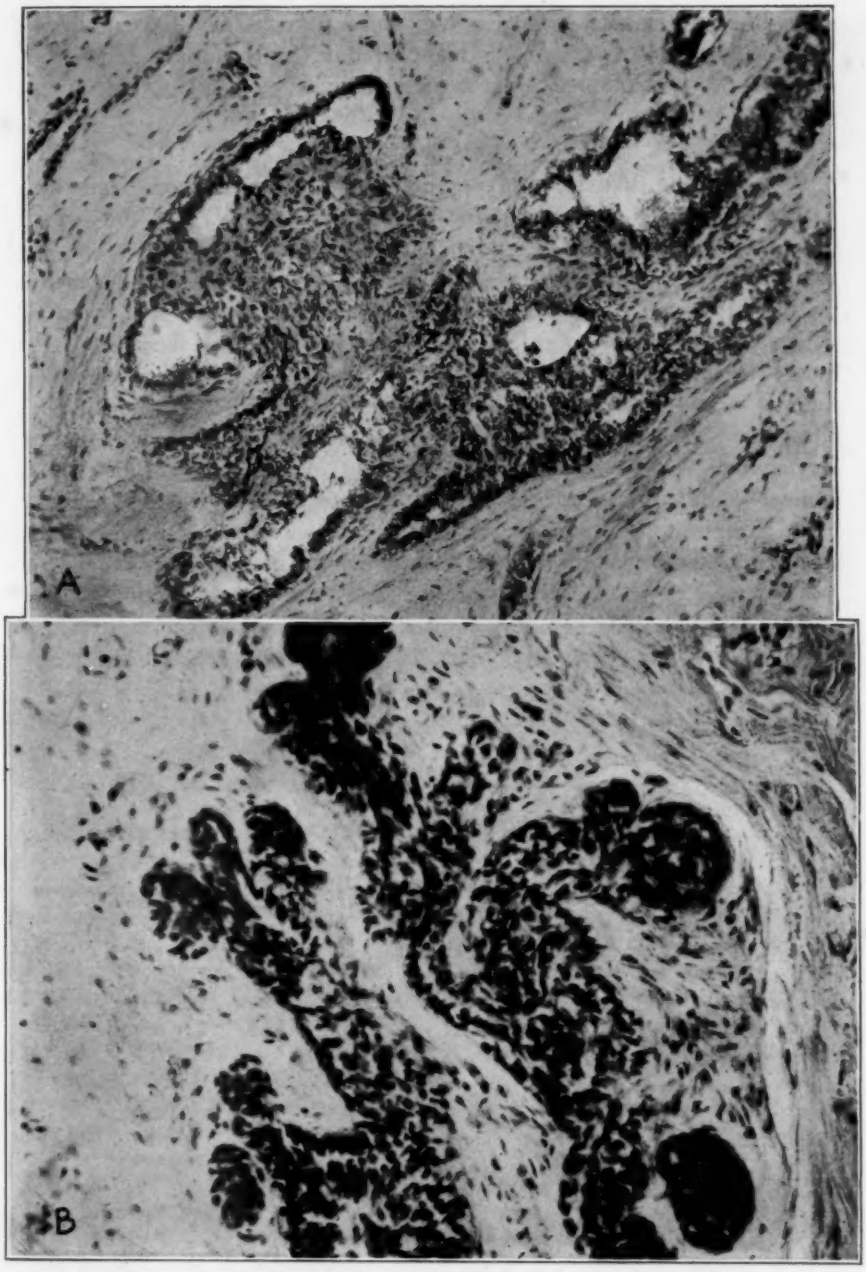


Fig. 3.—*A*, atypia. After simple mastectomy (case 23) there has been no recurrence for fourteen years. *B*, atypia. Simple mastectomy was performed (case 25), and the patient has been well for eleven years.

rences; the lesion was excised and showed the typical picture of simple chronic cystic mastitis. During the twelve years which have followed her last operation no tumor has reappeared. The remaining 23 patients of the series are completely cured after the local excision.

## CONCLUSIONS

There is no unanimity of opinion in the literature concerning the nature of chronic cystic mastitis, its relation to cancer of the breast or the best method of treatment. For more than twenty years the treatment of chronic cystic mastitis in this hospital has been governed by the histologic type of the lesion. Simple chronic cystic mastitis, which is present in more than 80 per cent of cases, is treated by local excision of the involved area only, and regular follow-up examinations of the patient are regarded as unnecessary. The second type, chronic cystic mastitis with papillary proliferation (4 per cent), is also treated with local removal, but the patient is advised to report for a clinical examination every six months after the operation. For the third type, chronic cystic mastitis with atypia (15 per cent), simple mastectomy and regular postoperative follow-up examination are recommended.

Twenty-six patients with chronic cystic mastitis of various types were treated according to these principles and followed for from ten to seventeen years after operation. Carcinoma of the breast did not develop in a single instance.

# NOCTURNAL GASTRIC SECRETION

## Studies on Normal Subjects and on Patients with Duodenal Ulcer, Gastric Ulcer and Gastric Carcinoma

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THE PURPOSE of this paper is to present the results of studies on the gastric secretion of normal persons and of patients with duodenal ulcer, gastric ulcer and gastric carcinoma. Henning and Norpoth,[1] Winkelstein[2] and Val Dez[3] observed a greater free acidity in the nocturnal secretion of patients with duodenal ulcer than in that of a normal group. Sandweiss and others,[4] on the other hand, concluded that male patients with uncomplicated duodenal ulcer do not secrete larger amounts of gastric juice than normal persons during the period from midnight to 7 a.m. It is difficult to compare the results obtained by these various workers inasmuch as varying methods of study were employed.

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Read in a Symposium on Peptic Ulcer at the joint meeting of the Section on Gastro-Enterology and Proctology and the Section on Surgery, General and Abdominal, at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, June 1947.

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Dragstedt and his co-workers [5] found that the average volume of the twelve hour continuous gastric secretion in 135 unselected patients with duodenal ulcer was 1,085 cc.; the average free acidity of the total nocturnal secretion was 55 clinical units. Thornton, Storer and Dragstedt [6] measured the nocturnal gastric secretion in patients with carcinoma of the stomach under similar conditions and found that the volume and free acidity of the total nocturnal gastric secretion were lower in this group than in patients with duodenal ulcer. Levin, Hamann and Palmer,[7] in similar studies, observed that the fasting twelve hour continuous nocturnal gastric secretion in 28 patients with uncomplicated duodenal ulcer on a Sippy regimen varied from 550 to 1,750 cc., the average amount being 1,110 cc. The free acidity of the total volume ranged from 18 to 122 clinical units, with an average of 62. To our knowledge similar studies on the continuous twelve hour nocturnal gastric secretion in normal healthy persons without gastrointestinal complaints have not been reported heretofore.

## METHODS

Fifty studies were made on 33 normal healthy persons who were known to have no gastrointestinal complaints, comprising thirty-three studies on 21 men and seventeen studies on 12 women. The ages ranged from 19 to 60 years; 1 subject was 19 years old, 20 were between 20 and 29 years, 11 were between 30 and 40 years and 1 was 60 years old (tables 1 and 2).

Seventy-four studies were made on 32 patients with duodenal ulcer (table 3), sixteen on 8 patients with gastric ulcer (table 4) and twenty-six on 12 patients with gastric carcinoma (table 5). The only criteria that governed the selection of patients was their ability to cooperate. In all patients the nature of the lesion was definitely proved by roentgenologic examination, gastroscopy or surgical exploration or a combination of all three. An ulcer crater was demonstrable roentgenologically in 22 patients with duodenal ulcer; abnormal gastric retention was present in 6. All the patients were admitted to the hospital because of distress attributed to peptic ulcer.

The number of patients studied with gastric ulcer and gastric carcinoma is obviously small. Nevertheless the data obtained to date are sufficiently constant to reveal certain trends. Craters were present in all patients with gastric ulcer; 2 patients had questionable obstruction of the pylorus. Ulceration was demonstrated in 6 of the patients with carcinoma of the stomach, and obstruction of the pylorus was present in 2.

The conditions under which the studies were made were identical except in one respect. The normal subjects were allowed to eat whatever they desired up to 12:30 p. m. on the day of the study, while the patients were given a clear liquid diet throughout the period of investigation. However, at 5:30 p. m. on the

5. Dragstedt, L. R.: Personal communication to the authors.

6. Thornton, F. T., Jr.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves, J. A. M. A. **130**:764 (March 23) 1946.

7. Levin, E.; Hamann, A., and Palmer, W. L.: The Effect of Radiation Therapy on the Nocturnal Gastric Secretion in Patients with Duodenal Ulcer, Proc. Central Soc. Clin. Research **19**:32, 1946; Gastroenterology **8**:565, 1947.

TABLE 1.—*Twelve Hour Continuous Nocturnal Gastric Secretion in Normal Men (8: 30 P. M. to 8: 30 A. M.)*

| Name | Age, Yr. | Volume, Cc. | Free Acid, Clinical Units | Hydrochloric Acid, Mg./Cc. | Total Hydrochloric Acid, Mg. |
|---|---|---|---|---|---|
| A. B. | 20 | 668 | 6 | 0.237 | 164.4 |
| | | 695 | 21 | 0.750 | 521.3 |
| G. McP. | 21 | 484 | 28 | 1.020 | 493.4 |
| O. T. | 23 | 613 | 25 | 0.911 | 558.7 |
| | | 464 | 42 | 1.734 | 804.5 |
| | | 657 | 64 | 2.361 | 1,551.4 |
| H. O. | 23 | 699 | 37 | 1.362 | 952.1 |
| | | 658 | 52 | 1.897 | 1,248.1 |
| J. D. | 23 | 522 | 16 | 0.591 | 308.4 |
| | | 567 | 48 | 1.746 | 989.9 |
| | | 436 | 47 | 1.728 | 753.5 |
| W. C. | 24 | 693 | 23 | 0.848 | 587.7 |
| | | 637 | 1 | 0.023 | 14.4 |
| D. E. | 24 | 211 | 28 | 1.027 | 216.7 |
| M. F. | 25 | 929 | 18 | 0.630 | 585.6 |
| J. F. | 27 | 173 | 29 | 1.041 | 180.1 |
| W. N. | 29 | 924 | 62 | 2.258 | 2,086.6 |
| M. B. | 30 | 433 | 41 | 1.496 | 647.6 |
| E. W. | 30 | 606 | 15 | 0.540 | 327.4 |
| | | 296 | 45 | 1.640 | 485.5 |
| P. H. | 31 | 752 | 24 | 0.880 | 661.7 |
| | | 555 | 28 | 1.017 | 564.3 |
| R. F. | 31 | 685 | 17 | 0.620 | 424.7 |
| | | 841 | 10 | 0.379 | 318.6 |
| E. B. T. | 32 | 789 | 31 | 1.141 | 900.5 |
| | | 600 | 14 | 0.523 | 319.2 |
| R. M. | 32 | 598 | 5 | 0.181 | 108.0 |
| H. D. | 33 | 952 | 26 | 0.934 | 888.9 |
| | | 1,188 | 47 | 1.724 | 2,047.9 |
| B. C. | 36 | 701 | 7 | 0.255 | 178.7 |
| J. B. K. | 37 | 755 | 36 | 1.300 | 981.8 |
| G. D. | 38 | 1,042 | 90 | 3.279 | 3,416.5 |
| R. G. | 60 | 365 | 9 | 0.344 | 125.5 |

TABLE 2.—*Twelve Hour Continuous Nocturnal Gastric Secretion in Normal Women (8: 30 P. M. to 8: 30 A. M.)*

| Name | Age, Yr. | Volume, Cc. | Free Acid, Clinical Units | Hydrochloric Acid, Mg./Cc. | Total Hydrochloric Acid, Mg. |
|---|---|---|---|---|---|
| A. S. | 19 | 773 | 13 | 0.475 | 366.8 |
| | | 705 | 4 | 0.148 | 104.0 |
| P. N. | 20 | 908 | 75 | 2.743 | 2,476.9 |
| | | 719 | 68 | 2.459 | 1,767.9 |
| J. J. | 21 | 294 | 18 | 0.665 | 195.5 |
| C. B. | 22 | 554 | 3 | 0.123 | 67.9 |
| | | 189 | 3 | 0.118 | 22.3 |
| E. S. | 22 | 351 | 51 | 1.862 | 653.6 |
| M. B. | 23 | 301 | 6 | 0.245 | 73.7 |
| R. M. | 23 | 148 | 29 | 1.059 | 156.7 |
| M. H. | 23 | 575 | 5 | 0.194 | 111.7 |
| | | 318 | 6 | 0.236 | 75.0 |
| R. H. | 24 | 242 | 37 | 1.579 | 382.2 |
| V. L. | 24 | 492 | 40 | 1.457 | 716.7 |
| Z. P. | 30 | 353 | 34 | 1.230 | 434.3 |
| | | 497 | 28 | 1.026 | 510.1 |
| W. E. | 32 | 407 | 36 | 1.321 | 537.6 |

TABLE 3.—*Twelve Hour Continuous Nocturnal Gastric Secretion in Patients with Duodenal Ulcer (8: 30 P. M. to 8: 30 A. M.)*

| Name | Age, Yr. | Duration of Symptoms | Volume, Cc. | Free Acid, Clinical Units | Hydrochloric Acid, Mg./Cc. | Total Hydrochloric Acid, Mg. |
|---|---|---|---|---|---|---|
| A. W. | 21 | 4 yr. | 1,000 | 79 | 2.859 | 2,858.6 |
| | | | 1,228 | 80 | 2.921 | 3,586.7 |
| W. M. | 23 | 5 yr. | 1,694 | 55 | 1.989 | 3,368.7 |
| | | | 1,440 | 43 | 1.576 | 2,268.9 |
| P. F. | 29 | 8 yr. | 1,222 | 43 | 1.568 | 1,915.9 |
| | | | 1,147 | 58 | 1,914 | 2,195.0 |
| | | | 1,150 | 13 | 0.482 | 553.8 |
| G. R. | 31 | 4 yr. | 1,178 | 33 | 1.198 | 1,411.4 |
| | | | 1,118 | 72 | 2.552 | 2,853,3 |
| A. B. | 31 | 10 yr. | 799 | 54 | 1.945 | 1,554.1 |
| | | | 858 | 51 | 1,864 | 1,599.0 |
| | | | 1,064 | 48 | 1.737 | 1,848.6 |
| R. S. | 31 | 9 yr. | 1,071 | 63 | 2.281 | 2,443.2 |
| | | | 990 | 75 | 2.727 | 2,699.8 |
| | | | 859 | 52 | 1.896 | 1,628.4 |
| F. H. | 35 | 12 yr. | 1,550 | 93 | 3.410 | 5,285.6 |
| | | | 1,567 | 96 | 3.473 | 5,442.2 |
| | | | 1,500 | 93 | 3.368 | 5,051.9 |
| E. H. | 37 | 10 yr. | 977 | 76 | 2.770 | 2,706.2 |
| | | | 896 | 71 | 2.597 | 2,327.1 |
| | | | 750 | 46 | 1.689 | 1,267.0 |
| J. R. | 39 | 4 yr. | 1,399 | 64 | 2,320 | 3,245.2 |
| | | | 1,460 | 50 | 1.818 | 2,653.6 |
| P. Y. | 39 | 7 yr. | 630 | 35 | 1.280 | 806.2 |
| | | | 675 | 38 | 1.392 | 939.9 |
| S. R. | 39 | 10 yr. | 1,205 | 60 | 2.170 | 2,615.1 |
| | | | 1,093 | 58 | 2.111 | 2,307.6 |
| | | | 775 | 44 | 1.610 | 1,247.4 |
| G. A. | 41 | 15 yr. | 760 | 46 | 1.659 | 1,261.1 |
| | | | 742 | 36 | 1.310 | 971.7 |
| R. H. | 42 | 16 yr. | 1,633 | 55 | 1.987 | 3,245.3 |
| | | | 1,780 | 69 | 2.521 | 4,488.0 |
| W. H. | 44 | 16 yr. | 956 | 72 | 2.613 | 2,498.2 |
| | | | 1,145 | 77 | 2.788 | 3,192.1 |
| | | | 1,585 | 38 | 1.400 | 2,278.8 |
| J. D. | 45 | 25 yr. | 965 | 46 | 1.679 | 1,653.7 |
| | | | 893 | 71 | 2.567 | 2,292.4 |
| J. G. | 45 | 1 yr. | 437 | 28 | 1.021 | 446.3 |
| | | | 419 | 45 | 1.634 | 684.6 |
| S. N.* | 46 | 9 mo. | 1,187 | 26 | 0.933 | 1,107.6 |
| | | | 550 | 61 | 2.204 | 1,212.4 |
| N. W. | 48 | 30 yr. | 1,041 | 36 | 2.053 | 2,136.7 |
| | | | 1,482 | 63 | 2.365 | 3,505.5 |
| D. H. | 48 | 25 yr. | 963 | 61 | 1.837 | 1,768.7 |
| | | | 539 | 27 | 0.968 | 521.9 |
| | | | 661 | 27 | 0,967 | 639.4 |
| D. D. | 48 | 22 yr. | 824 | 61 | 2.225 | 1,833.0 |
| | | | 806 | 72 | 2.609 | 2,103.2 |
| C. O. | 50 | 13 yr. | 1,403 | 88 | 3.201 | 4,491.5 |
| | | | 1,839 | 85 | 3.105 | 5,710.7 |
| H. G. | 50 | 13 yr. | 1,380 | 82 | 2,966 | 4,120.5 |
| | | | 1,047 | 86 | 3.114 | 3,259.8 |
| O. H. | 51 | 6 yr. | 906 | 38 | 1.384 | 1,253.8 |
| | | | 798 | 76 | 2.749 | 2,193.9 |
| F. H. | 52 | 10 yr. | 729 | 82 | 2.971 | 2,165.5 |
| | | | 988 | 68 | 2.489 | 2,459.2 |
| J. S. | 54 | 20 yr. | 920 | 64 | 2.432 | 2,237.3 |
| | | | 1,001 | 77 | 2.792 | 2,794.3 |
| F. Z. | 55 | 11 yr. | 522 | 64 | 2.326 | 1,214.0 |
| | | | 362 | 86 | 3.129 | 1,132.7 |
| F. H. | 56 | 7 yr. | 1,615 | 45 | 1.625 | 2,623.6 |
| | | | 1,400 | 51 | 1.844 | 2,582.1 |
| J. G. | 59 | 6 yr. | 726 | 23 | 0.847 | 615.0 |
| | | | 398 | 43 | 1.562 | 621.7 |
| E. M. | 61 | 1½ yr. | 940 | 112 | 4.072 | 3,827.8 |
| | | | 1,396 | 97 | 3.525 | 4,921.1 |
| | | | 1,262 | 70 | 2.544 | 3,210.9 |
| R. J. | 61 | 2 yr. | 498 | 36 | 1.302 | 648.3 |
| | | | 393 | 38 | 1.380 | 543.6 |
| P. C. | 69 | 25 yr. | 574 | 39 | 1.425 | 817.9 |
| | | | 503 | 42 | 1.534 | 771.6 |
| F. H. | 70 | 5 mo. | 620 | 78 | 2.842 | 1,761.7 |
| | | | 537 | 81 | 2.956 | 1,587.3 |
| | | | 889 | 59 | 2.134 | 1,896.8 |

* This patient was a woman.

day of the study all subjects were given an identical meal containing 37 Gm. of carbohydrate, 3 Gm. of protein and no fat. Food or water was not permitted thereafter. At 8:00 p. m. a Levine tube was introduced through the nose into

TABLE 4.—*Twelve Hour Continuous Nocturnal Gastric Secretion in Patients with Gastric Ulcer (8:30 P. M. to 8:30 A. M.)*

| Name | Age, Yr. | Duration of Symptoms | Volume, Cc. | Free Acid, Clinical Units | Hydrochloric Acid, Mg./Cc. | Total Hydrochloric Acid, Mg. |
|---|---|---|---|---|---|---|
| A. P. | 47 | 2 yr. | 202 | 0 | 0 | 0 |
| | | | 594 | 3 | 0.094 | 56.1 |
| H. A. | 47 | 25 yr. | 861 | 12 | 0.425 | 365.6 |
| | | | 566 | 6 | 0.204 | 115.5 |
| A. Z. | 49 | 19 yr. | 736 | 3 | 0.113 | 83.0 |
| | | | 719 | 5 | 0.167 | 120.0 |
| M. C.* | 34 | 8 yr. | 558 | 35 | 1.267 | 700.5 |
| | | | 524 | 37 | 1.363 | 713.9 |
| I. B. | 57 | 3 wk. | 1,122 | 3 | 0.104 | 116.1 |
| | | | 1,014 | 11 | 0.417 | 422.8 |
| V. L. | 58 | 18 yr. | 385 | 14 | 0.519 | 199.8 |
| | | | 335 | 2 | 0.072 | 23.9 |
| | | | 374 | 0 | 0 | 0 |
| J. W. | 60 | 10 yr. | 432 | 11 | 0.040 | 17.0 |
| | | | 531 | 5 | 0.198 | 105.0 |
| J. M. | 60 | 1 yr. | 1,018 | 36 | 1.306 | 1,329.4 |

* This patient was a woman.

TABLE 5.—*Twelve Hour Continuous Nocturnal Gastric Secretion in Patients with Gastric Carcinoma (8:30 P. M. to 8:30 A. M.)*

| Name | Age, Yr. | Duration of Symptoms | Volume, Cc. | Free Acid, Clinical Units | Hydrochloric Acid, Mg./Cc. | Total Hydrochloric Acid, Mg. |
|---|---|---|---|---|---|---|
| H. P. | 45 | 1 yr. | 457 | 0 | 0 | 0 |
| | | | 627 | 32 | 1.148 | 719.4 |
| | | | 320 | 13 | 0.466 | 149.0 |
| J. V. P. | 48 | 2 yr. | 588 | 7 | 0.256 | 150.4 |
| | | | 464 | 8 | 0.307 | 142.5 |
| O. R. | 49 | 5 mo. | 587 | 5 | 0.193 | 113.3 |
| J. W. | 55 | 6 mo. | 1,243 | 0 | 0 | 0 |
| | | | 377 | 0 | 0 | 0 |
| B. K. | 57 | 9 yr. | 296 | 0 | 0 | 0 |
| | | | 571 | 0 | 0 | 0 |
| W. K. | 58 | 5 wk. | 518 | 0 | 0 | 0 |
| | | | 355 | 0 | 0 | 0 |
| F. Z. | 59 | 3 yr. | 586 | 14 | 0.519 | 304.4 |
| | | | 332 | 9 | 0.330 | 110.1 |
| | | | 296 | 1 | 0.005 | 1.5 |
| | | | 453 | 3 | 0.129 | 58.2 |
| E. Z.* | 60 | 10 mo. | 205 | 2 | 0.054 | 11.0 |
| | | | 295 | 1 | 0.028 | 8.4 |
| J. L. | 60 | 6 mo. | 375 | 7 | 0.231 | 86.9 |
| | | | 311 | 0 | 0 | 0 |
| J. C. | 61 | 2 yr. | 250 | 14 | 0.507 | 131.3 |
| | | | 290 | 13 | 0.473 | 137.1 |
| | | | 322 | 1 | 0.017 | 5.4 |
| A. E. | 66 | 1 yr. | 446 | 0 | 0 | 0 |
| | | | 472 | 0 | 0 | 0 |
| T. D. | 67 | 1½ yr. | 288 | 0 | 0 | 0 |

* This patient was a woman.

the stomach. The position of the tube was checked in each case by fluoroscopic examination. The stomach was then completely emptied. At 8:30 p. m. continuous suction was initiated and maintained until 8:30 a. m. the following morning. The

Wangensteen apparatus was modified so that the specimen bottles could be changed easily and rapidly every hour throughout the entire twelve hour period. As a rule this procedure did not interfere with the subject's sleep, although several complained of some discomfort of the nose and throat. No antispasmodics, secretory depressants or sedation of any kind were given. Whenever the duodenal regurgitation into the stomach was sufficient to color the aspirated material dark green, the specimen was discarded. The volume and free acidity of each hourly sample were determined by the usual methods. The hydrochloric acid was computed in milligrams from these values.

## RESULTS

*Volume of the Twelve Hour Nocturnal Gastric Secretion (table 6, fig. 1).*—The twelve hour continuous fasting secretion in 33 normal subjects varied considerably. The volume for the group ranged from 148 to 1,188 cc., with an average of 581 cc. The average volume secreted by the male subjects was greater than that of the female sub-

TABLE 6.—*Range and Average Volume of the Twelve Hour Nocturnal Gastric Secretion in Normal Subjects and in Patients with Duodenal Ulcer, Gastric Ulcer and Gastric Carcinoma*

| | Number of Patients | Number of Studies | Volume in Cubic Centimeters | | |
|---|---|---|---|---|---|
| | | | Range | | |
| | | | Minimum | Maximum | Average |
| Normal | | | | | |
| Male | 21 | 33 | 173 | 1,188 | 643 |
| Female | 12 | 17 | 148 | 903 | 460 |
| Total | 33 | 50 | 148 | 1,188 | 581 |
| Duodenal ulcer | 32 | 74 | 362 | 1,839 | 1,004 |
| Gastric ulcer | 8 | 16 | 202 | 1,122 | 623 |
| Gastric carcinoma | 12 | 26 | 205 | 1,243 | 436 |

jects. For the former the volume varied from 173 to 1,188 cc., with an average of 643 cc., while for the latter the range was 148 to 903 cc., with an average of 460 cc. The volume was less than 800 cc. in 86 per cent of the studies and below 600 cc. in 50 per cent.

Seventy-four studies were made on 32 patients (31 men and 1 woman) with duodenal ulcer. The total volume of the secretion ranged from 362 to 1,839 cc., with an average of 1,004 cc. The volume was less than 800 cc. in only 32 per cent of the studies. The volume exceeded 1,000 cc. in 47 per cent of the studies as compared to only 4 per cent of those on the normal group.

The results in the 8 patients with gastric ulcer are also shown in table 6 and figure 1. The range was from 202 cc. to 1,122 cc., with an average of 623 cc. The volume was less than 800 cc. in 75 per cent of the studies and below 600 cc. in more than 50 per cent.

The volume in the patients with carcinoma of the stomach ranged from 205 cc. to 1,243 cc., with an average of 436 cc. It was less than 800 cc. in 96 per cent of the studies and below 400 cc. in more than 50 per cent.

*Free Acidity of the Twelve Hour Nocturnal Gastric Secretion (table 7, fig. 2).*—The free acidity of the total nocturnal secretion varied in the four groups studied. In the normal subjects it ranged from 1.0 clinical unit to as high as 90 clinical units, the average being 29. There

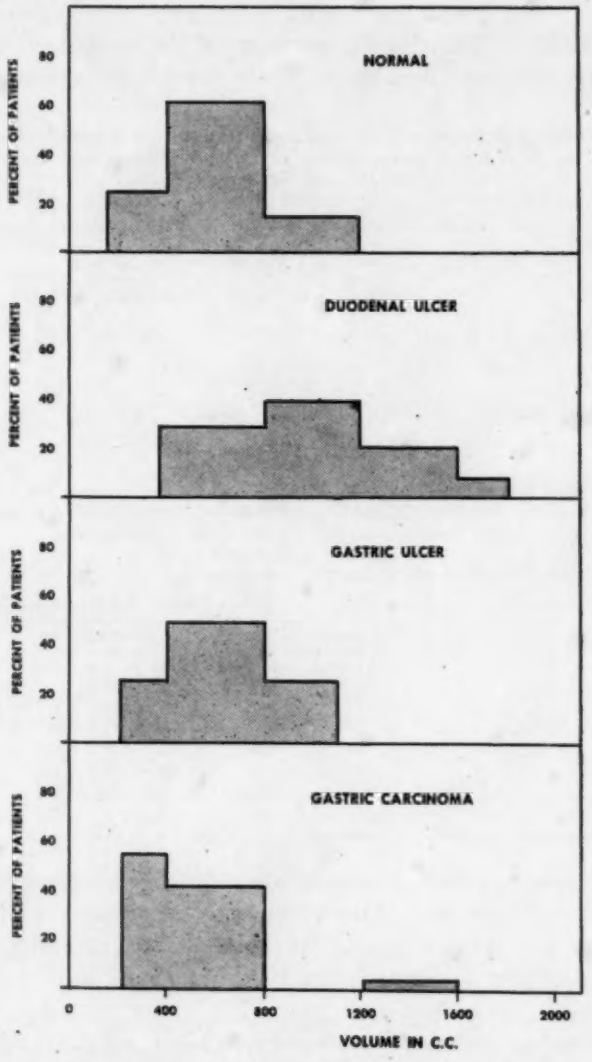


Fig. 1.—Distribution of total volume of twelve hour nocturnal gastric secretion.

was no significant difference between men and women. There was no instance of persistent achlorhydria in all the hourly specimens. The free acidity was less than 40 clinical units in 72 per cent of the studies and less than 30 units in over 50 per cent. In contrast only 20 per cent

of the patients with duodenal ulcer had an acidity below 40 clinical units; values of 60 clinical units or more were obtained in 50 per cent. The values for free hydrochloric acid varied widely, the range being from 13 to 112 clinical units, with an average of 61.

The acidity was less than 40 clinical units in all patients with gastric ulcer and gastric carcinoma. Anacidity was observed in the total nocturnal secretion in 13 per cent of the studies on the group with ulcers, although in none of them was it persistent when the

TABLE 7.—*Range and Average Free Acidity of the Twelve Hour Nocturnal Gastric Secretion in Normal Subjects and in Patients with Duodenal Ulcer, Gastric Ulcer and Gastric Carcinoma*

| | Number of Patients | Number of Studies | Free Acidity in Clinical Units | | |
|---|---|---|---|---|---|
| | | | Range | | |
| | | | Minimum | Maximum | Average |
| Normal | | | | | |
| Male | 21 | 33 | 1.0 | 90 | 30 |
| Female | 12 | 17 | 3.0 | 72 | 27 |
| Total | 33 | 50 | 1.0 | 90 | 29 |
| Duodenal ulcer | 32 | 74 | 13.0 | 112 | 61 |
| Gastric ulcer | 8 | 16 | 0.0 | 37 | 12 |
| Gastric carcinoma | 12 | 26 | 0.0 | 32 | 5 |

TABLE 8.—*Range and Average Total Amount of Free Hydrochloric Acid in the Twelve Hour Nocturnal Gastric Secretion in Normal Subjects and in Patients with Duodenal Ulcer, Gastric Ulcer and Gastric Carcinoma*

| | Number of Patients | Number of Studies | Total Free Hydrochloric Acid, Mg. | | |
|---|---|---|---|---|---|
| | | | Range | | |
| | | | Minimum | Maximum | Average |
| Normal | | | | | |
| Male | 21 | 33 | 14 | 3,417 | 740 |
| Female | 12 | 17 | 22 | 2,477 | 509 |
| Total | 33 | 50 | 14 | 3,417 | 661 |
| Duodenal ulcer | 32 | 74 | 446 | 5,711 | 2,242 |
| Gastric ulcer | 8 | 16 | 0 | 1,329 | 273 |
| Gastric carcinoma | 12 | 26 | 0 | 719 | 82 |

aspirations were repeated on successive nights. In contrast achlorhydria was present in 42 per cent of the group with carcinoma; in 33 per cent the anacidity was persistent in all specimens on two consecutive nights. The amount of free acid was below 10 clinical units in 81 per cent of this group.

*Total Amount of Free Hydrochloric Acid in the Twelve Hour Nocturnal Gastric Secretion (table 8, fig. 3).*—In the normal subjects the amount of free hydrochloric acid secreted during the night averaged 661 mg. The minimum value was 14 mg. and the maximum as high as 3,417 mg. The average output of hydrochloric acid during the night was greater in the male subjects than in the female subjects. In the entire group the total output was less than 1,000 mg. in 84 per cent

of the studies and below 500 mg. in approximately 50 per cent. In contrast, in 81 per cent of the studies on patients with duodenal ulcer the amount secreted was more than 1,000 mg., and in over 50 per cent it was in excess of 2,000 mg. The average total output for patients with duodenal ulcer was 2,242 mg., the range being from 446 to 5,711 mg.

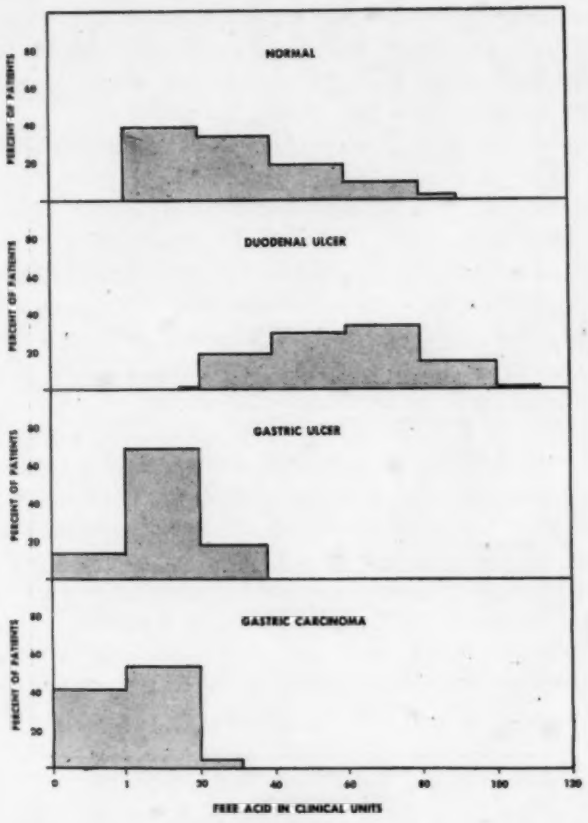


Fig. 2.—Distribution of free hydrochloric acid in the twelve hour nocturnal gastric secretion.

The average amount of free hydrochloric acid secreted by patients with gastric ulcer was 273 mg. Only 1 patient in this group secreted more than 1,000 mg. The amount was less than 500 mg. in 81 per cent of the studies.

All the patients with gastric carcinoma studied to date secreted less than 1,000 mg. of hydrochloric acid during the night. The amount was less than 500 mg. in 96 per cent of the observations. Of the latter group, 44 per cent had achlorhydria, 24 per cent excreted less than 100 mg. of hydrochloric acid and 28 per cent excreted between 100 and 150 mg. The average for the entire group was 82 mg.

## COMMENT

This study demonstrates that there are statistically significant differences between the gastric secretion of normal persons and that of patients with duodenal ulcer, gastric ulcer and carcinoma, although, as one would expect, there is an overlapping.[8]

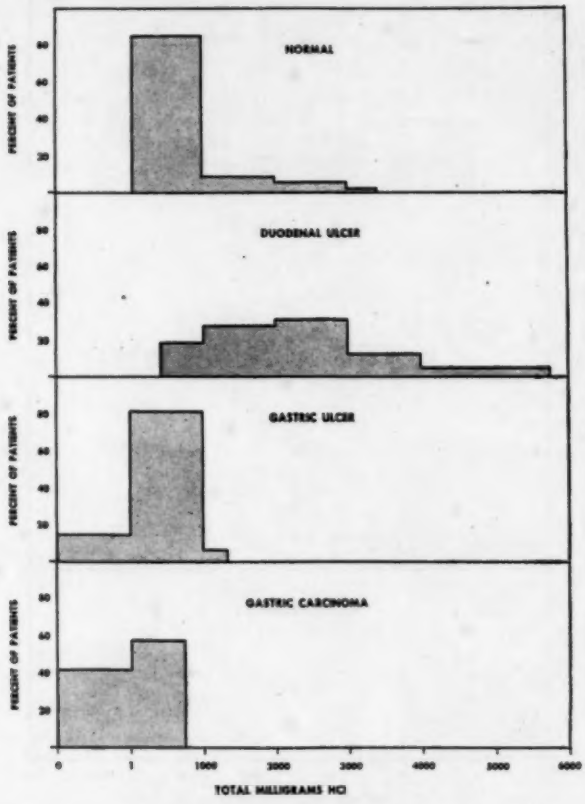


Fig. 3.—Distribution of total hydrochloric acid (milligrams) in the twelve hour nocturnal gastric secretion.

The volume of the continuous nocturnal gastric secretion in the group with duodenal ulcers is significantly higher than that in normal subjects. Comparison of the normal group with the small series of patients with gastric ulcer and gastric carcinoma indicates that there is no significant difference in the volume of gastric juice secreted between normal subjects and those with gastric ulcer. Patients with gastric carcinoma tend to secrete a lower volume of gastric juice than

8. Herbert D. Landahl, assistant professor of mathematical biophysics, aided in the statistical analysis of the data.

do normal persons. The continuous nocturnal gastric secretion in patients with duodenal ulcer is much greater than that encountered in patients with either gastric carcinoma or gastric ulcer. Patients with gastric ulcer, on the average, secrete a greater volume than do patients with gastric carcinoma.

Similarly, the free acidity of the total nocturnal gastric secretion is much higher in patients with duodenal ulcer than in normal subjects. On the other hand, the free acidity tends to be lower in patients with gastric ulcer and gastric carcinoma than in normal persons. The free acidity of the nocturnal gastric secretion tends to be higher in patients with gastric ulcer than in patients with carcinoma.

The differences in gastric secretion between the groups studied are most evident with regard to the total amount of hydrochloric acid secreted during the night. Those with duodenal ulcer secrete a significantly greater amount of hydrochloric acid than do normal persons. On the other hand normal persons secrete more hydrochloric acid in the nocturnal gastric secretion than do patients with either gastric ulcer or gastric carcinoma; in both instances the differences are significant. Patients with gastric carcinoma tend to secrete less hydrochloric acid than do patients with gastric ulcer.

The results also indicate a wide individual variation in the volume of gastric secretion and in the output of free hydrochloric acid even in the same person. However, if the "correlation coefficient" is computed, it becomes apparent that a person with a high secretion on one night will in the majority of instances have a high gastric secretion on successive nights. The same constancy is demonstrated by persons with a low secretory rate.

Sippy,[9] Palmer [10] and Winkelstein [2] have pointed out that the great difficulty in ulcer therapy is the control of the excessive continued nocturnal secretion. Dragstedt [5] maintains "that the chief abnormality of duodenal ulcer patients lies not in the fact that they secrete more gastric juice in response to the stimulus of histamine or alcohol than do normal individuals but rather in the fact that they secrete large volumes of highly acid gastric juice when there is no known stimulus to the gastric secretory mechanism." The present data quantitatively confirm these observations with respect to duodenal ulcer, not for gastric ulcer, and are similar to those obtained in the studies of Dragstedt and

9. Sippy, B. W.: Gastric and Duodenal Ulcer, J. A. M. A. **64**:1625 (May 15) 1915.

10. Palmer, W. L.: Fundamental Difficulties in the Treatment of Peptic Ulcer, J. A. M. A. **101**:1604 (Nov. 18) 1933. Palmer, W. L., and Templeton, F. E.: The Effect of Radiation Therapy on Gastric Secretion, ibid. **112**:1429 (April 15) 1939.

his co-workers [11]; the two studies were carried out under the same conditions. In a previous investigation Levin, Hamann and Palmer [7] found that for 28 patients with uncomplicated duodenal ulcer the average volume of the continuous nocturnal gastric secretion was 1,110 cc., with an average free acidity of 62 clinical units. The earlier work differs from the present one in two respects: first, all the patients had uncomplicated duodenal ulcer whereas 6 of the present group had abnormal gastric retention; second, all the patients in the earlier study were placed on a Sippy regimen while the tests were being made whereas in the present investigation the patients were given a clear liquid diet. Nevertheless the average volume and the average free acidity were similar in the two groups, the difference being only 1.0 clinical unit. It can be safely concluded therefore that the average volume of the continuous nocturnal gastric secretion in patients with duodenal ulcer is between 1,000 and 1,100 cc. and that the average free acidity is approximately 60 clinical units.

We are not able to advance at this time a satisfactory explanation for the difference between our results and those obtained by Sandweiss and his co-workers. The methods and conditions of study were similar but not identical. As nearly as we can compare the results, Sandweiss obtained comparatively higher values for the normal subjects and lower values for those with duodenal ulcer. It may be significant that Sandweiss's normal subjects were all medical students; the highest "normal" values obtained by us were obtained for medical students and graduates and the lowest for nonmedical personnel.

It is of interest to compare the results in the group with carcinoma with those obtained by Thornton, Storer and Dragstedt,[6] since the two studies were made under similar conditions. Although the average volume of secretion was slightly higher in the present group, the average free acidity was remarkably similar.

## SUMMARY

The volume and the hydrochloric acid content of the nocturnal gastric secretion in patients with duodenal ulcer, gastric ulcer and gastric carcinoma are compared with those for normal subjects. The data indicate that the volume and output of hydrochloric acid are usually highest in patients with duodenal ulcer. For a small series of patients with gastric ulcer the average volume of gastric juice was approximately the same as that for normal subjects, but the average content of hydrochloric acid was lower. Nocturnal gastric secretion was lower in patients with carcinoma of the stomach than in normal persons. The nocturnal gastric secretion in patients with gastric carcinoma was less than that in patients with gastric ulcer.

11. Dragstedt.[5] Thornton, Storer and Dragstedt.[6]

# SURGICAL APPROACH TO HYPERTENSIVE VASCULAR DISEASE

## Technic of Operation, Discussion of Complications and Method of Prevention

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DILATATION of the capillary bed allows the same volume of blood to flow through larger tubes, with resulting fall in blood pressure. Pressor drugs temporarily reverse the process and cause blood pressure to rise.[1] Splanchnicectomy and sympathectomy appear to serve a dual purpose, namely, that of producing vasodilatation of the splanchnic visceral bed and of the capillary bed of the lower limbs and release of sympathetic control to the kidneys and adrenals through the aorticorenal ganglion, which, it is believed, controls the secretion of renin and the emotional internal secretion of epinephrine,[2] powerful pressor substances. At present, however, it is felt that the pituitary body, the thalamus and the thyroid are all involved in the condition of hypertensive vascular disease,[3] on which our present approach by means of sympathectomy has but slight influence. The surgical procedure is therefore mechanical for the greater part, but it is the best therapy which can be offered as a means of lowering the ceiling pressure and of preventing too high an emotional rise in systolic pressure. It is by no means the ultimate goal in the treatment of this disease. Search for the cause of hypertension shall continue to be made in the future.

### SELECTION OF CASES

Cases of hypertensive vascular disease may be selected and classified as belonging to groups 1, 2, 3 and 4 and as cases of rapidly progressing hypertensive vascular disease. It must be borne in mind, however,

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1. Pickering, G. W.: The Peripheral Resistance in Persistent Arterial Hypertension, Clin. Sc. **2**:209-235, 1935.

2. White, H. L.; Heinbecker, P., and Rolf, D.: Some Endocrine Influences on Renal Function and Cardiac Output, Am. J. Physiol., to be published.

3. Heinbecker, P.: Factors Limiting Surgery for Essential Hypertension, Ann. Surg. **126**:535-543, 1947. Pickering, G. W.; Kissin, M., and Rothchild, P.: Relationship of Carotid Sinus Mechanism to Persistent High Blood Pressure in Man, Clin. Sc. **2**:193-200, 1936.

that this classification is only relative. The possibility of complications and sequelae of hypertensive vascular disease, such as anginal attacks, myocardial degeneration, cerebral spasms or cerebral hemorrhage, pontile hemorrhage and retinal hemorrhage, increases operative risk. In my opinion, anginal attacks or myocardial breakdown increases the risk (although there is no evidence at the time of examination) to such an extent that I believe operation should be refused as a therapeutic measure.

In the cases in group 4 the condition is verging on rapidly progressing hypertensive vascular disease. Since the outlook is extremely grave, the patients should be given the benefit of operation even though operation will only prolong life for an average of three to five years.

Extreme elevation of the systolic blood pressure is not a contraindication to surgical treatment whereas a diastolic blood pressure of 140 which does not decrease with three days of rest in bed is an ill omen.

It is taken for granted in the selection of the cases in groups 1, 2, 3 and 4 that the renal function is satisfactory, with a urea clearance or a concentration factor of 40 or better. Moderate pyelitis is not a contraindication. It has been found, however, that patients with a history of albuminuria for ten or more years in spite of apparently normal renal function are subject to renal failure, which results in anuria, uremia and death. A rapid postoperative rise of the blood urea nitrogen from normal to approximately 90 mg. per hundred cubic centimeters in twelve hours is fatal. Possibly the rise in blood urea nitrogen is too rapid to be tolerated, since in medical uremia the level will frequently rise to 200 mg. before death occurs.

The prognosis varies directly with the selection of cases,[4] the response of the systolic and diastolic blood pressure to three days of rest in bed, and the approximation to normal of systolic and diastolic pressure following the intravenous injection of 3 cc. of tetraethylammonium chloride in doses of 1 cc. one minute apart or of 5 cc. in refractory cases. The more labile the capillary bed, the better the prognosis for relief of the symptoms of hypertension. Tetraethylammonium chloride appears to give a better idea of prognosis than "sodium amytal," the nitrites or "pentathol sodium." It is more simple to administer and does not appear to produce any reactions in the patient. The blood pressure curve produced by the administration of tetraethylammonium chloride corresponds favorably with the final results obtained by a two stage thoracolumbar splanchnicectomy and sympathectomy after a lapse of six months to a year. The following 13 cases illustrate the points referred to with reference to the "etamon chloride" (tetraethylammonium chloride) test.

4. Grimson, K. S.: Sympathectomy and Circulation—Anatomic and Physiologic Considerations and Early and Late Limitations, Surgery **19**:277-298, 1946.

CASE 1.—Mrs. C. C., aged 30 and weighing 110 pounds (50 Kg.), had hypertensive vascular disease stimulated by her first pregnancy. On her admission to the hospital, on Sept. 18, 1946, the blood pressure was 200 systolic and 103 diastolic. On Sept. 24, 1946, it was 155 systolic and 120 diastolic, and after an "etamon chloride" test on September 26, it dropped from 204 systolic and 130 diastolic to 140 and 104. There was no effect on the gastrointestinal tract; slight stinging of the sclera, no irritation of the bladder and no cutaneous reaction. The first stage operation was performed on October 8 and the second stage operation on October 29. The first operation involved the area from the sixth dorsal to the second lumbar vertebra. The second stage involved the area from the eighth dorsal to the second lumbar vertebra, including all splanchnic nerves. The blood pressure on discharge from the hospital was 130 systolic and 70 diastolic with the patient lying down. On July 15, 1947, she was well. The blood pressure was 110 systolic and 80 diastolic. An "etamon chloride" test showed that there was a definite lability of the blood vessels. It gave a definite indication for operation, but it showed that the results of operation were more complete than those of interruption of the sympathetic chain by the use of "etamon chloride."

CASE 2.—Mrs. H. L., aged 59, had hypertensive vascular disease complicated by diabetes with headaches and dizzy spells. Her blood pressure on Oct. 28, 1946, was 240 systolic and 138 diastolic, and after an "etamon chloride" test on October 31 it dropped from 210 systolic and 124 diastolic to 120 and 84. The first stage of the operation was on November 5 and the second stage on March 27, 1947. The patient got relief from the headaches and slight dizziness resulting from hypotension. Eight months after the second operation the blood pressure was approximately 140 systolic and 90 diastolic.

CASE 3.—Mrs. A. D., aged 39 years and weighing 110 pounds (50 Kg.), suffered from hypertensive vascular disease. Her blood pressure on admission to the hospital was 200 systolic and 105 diastolic. After the administration of "etamon chloride" on Nov. 2, 1946, it dropped from 192 systolic and 130 diastolic to 142 and 110. The first stage operation was performed on November 5 and the second stage operation on March 5, 1947. The patient was discharged after the first stage with a blood pressure of 170 systolic and 120 diastolic, but she subsequently came back in March for the second operation and was discharged with a blood pressure of 135 systolic and 90 diastolic. Again the close correlation between the results of the use of "etamon chloride" and those of sympathectomy was seen but only after the second stage was completed.

CASE 4.—Mr. S. H., aged 46, had hypertensive vascular disease with headaches, dizziness on exertion, epistasis and elevation of the blood pressure. On his admission to the hospital, on Feb. 7, 1947, the blood pressure was 200 systolic and 120 diastolic. After an "etamon chloride" test on February 25, it came down from 210 systolic and 130 diastolic to 182 and 124. There were retinal changes, and the urea concentration factor was low. Subsequently the patient was considered a failure from the point of view of medical and surgical treatment. The effect of 6 cc. of "etamon chloride" was observed. This only reduced the pressure to 160 systolic and 130 diastolic. The patient was not operated on since the vessels were insufficiently labile, and he died of a cerebral accident three months later.

CASE 5.—Mrs. A. L., aged 52 and weighing 152 pounds (69 Kg.), had hypertensive vascular disease with excruciating headaches. The blood pressure on her admission to the hospital (Feb. 17, 1947) was 220 systolic and 120 diastolic. After an "etamon chloride" test on March 4 it was reduced from 216 systolic and 100 diastolic to 184 and 104, and after another test on March 7 it decreased from

212 systolic and 100 diastolic to 154 and 90. The first stage operation was done on April 25 and the second stage on May 27. The patient did well and left the hospital with a blood pressure of 140 systolic and 90 diastolic. There has been no subsequent check-up to find out what the blood pressure is at the present time. On November 24 it was 145 systolic and 90 diastolic.

Case 6.—Mr. J. B., aged 35 and weighing 140 pounds (63.5 Kg.), had rapidly progressing arteriolar nephrosclerosis. Hypertension had been present for two years, with severe headaches and renal damage. The blood pressure on his admission to the hospital (March 7, 1947) and after the use of "etamon chloride" was 220 systolic and 147 diastolic; this came down to 180 and 130. With the use of "etamon chloride" again on March 10 it came down from 242 systolic and 145 diastolic to 212 and 120. This patient was considered an extremely poor risk both from the point of view of renal function and of eye signs and from the fact that the vessels were not labile. He was therefore not operated on, and he died of cerebral hemorrhage about three weeks after leaving the hospital.

Case 7.—J. B., a woman aged 44 and weighing 110 pounds (50 Kg.), suffered from hypertensive vascular disease with headaches for years and shortness of breath for five years. A previous operation had been performed on the thyroid for hypertension. With an "etamon chloride" test on Nov. 13, 1946, the blood pressure dropped from 180 systolic and 100 diastolic to 150 and 95. The first stage operation was done on November 18, and the patient was discharged on December 10 with a blood pressure of 152 systolic and 90 diastolic lying down. She subsequently came back for the second stage in January 1947. Now, about ten months later, she has an approximate blood pressure of 150 systolic and 90 diastolic and is free of symptoms.

Case 8.—Mr. O. L., aged 40 and weighing 172 pounds (78 Kg.), suffered with hypertensive vascular disease for one year and occipital headaches for more than two years. On his admission to the hospital (Nov. 25, 1946) the blood pressure was 200 systolic and 120 diastolic, and with an "etamon chloride" test on November 29 it dropped from 200 systolic and 110 diastolic to 120 and 90. The first stage operation was done on December 2 and the second stage on Feb. 3, 1947. The patient was discharged from the hospital on March 12, 1947, with a blood pressure of 120 systolic and 95 diastolic lying down. It is interesting to note that the blood pressure came down after the use of "etamon chloride" and that after completion of the two stages it was approximately the same. Ten months postoperatively the blood pressure was 135 systolic and 90 diastolic.

Case 9.—Miss K. T., aged 39 and weighing 142 pounds (64 Kg.), suffered with hypertensive vascular disease. She has had headaches all her life, along with fatigue, shortness of breath and precordial pain. On her admission to the hospital her blood pressure (Dec. 9, 1946) was 240 systolic and 120 diastolic, and with an "etamon chloride" test on December 11 it dropped from 190 systolic and 130 diastolic to 120 and 90. The first stage operation was done on December 3 and the second stage on Jan. 3, 1947. Her blood pressure on discharge from the hospital on January 25 was 120 systolic and 90 diastolic. She sent in a report on August 15 to the effect that her blood pressure was 144 systolic and 90 diastolic during activity. A subsequent report in November gave the blood pressure as 144 systolic and 90 diastolic. She resumed duties as a surgical nurse in an operating room.

Case 10.—Miss R. S., aged 19 and weighing 142 pounds (64 Kg.), had hypertensive vascular disease of group 1. She suffered with headaches. The hypertension was discovered in a preemployment examination. On her admission to the hospital (Dec. 4, 1946) the blood pressure was 190 systolic and 115 diastolic and

on December 10 after the use of "etamon chloride" it came down from 175 systolic and 110 diastolic to 142 and 98. There was no effect on the gastrointestinal tract. There was a slight burning sensation of the eyes, no effect on the bladder and a temporary drying of the skin. The first stage operation was done on December 14 and the second stage on Jan. 27, 1947. The patient left the hospital with a blood pressure of 110 systolic and 70 diastolic lying down. On July 15 the standing pressure was 100 systolic and 70 diastolic. The sympathetic chain was removed from the sixth dorsal down through the second lumbar vertebra, including all splanchnic nerves. At the second stage of the operation the sympathetic chain from the eighth dorsal down through the second lumbar vertebra was removed as well as all splanchnic nerves. In November 1947 the blood pressure was 100 systolic and 70 diastolic. The patient is working as a salesgirl in a department store.

Case 11.—Miss E. S., aged 52 and weighing 130 pounds (59 Kg.), had hypertensive vascular disease with headaches, dizziness, vomiting and shortness of breath. On her admission to the hospital the blood pressure was 210 systolic and 130 diastolic. After an "etamon chloride" test (on Jan. 14, 1947) it was 208 systolic and 108 diastolic, and it came down to 110 systolic and 90 diastolic. The first stage operation was done on January 16 and the second stage on March 24. This patient was an exceptionally poor risk. She had had two or three mild hemiplegic attacks, and one hemiplegic attack occurred between the stages of the operation. Nevertheless she had less trouble than we expected, felt well and was discharged with a blood pressure of 135 systolic and 80 diastolic. An "etamon chloride" test showed a drop from 208 systolic and 108 diastolic to 110 and 70 whereas with the operative procedure there was a sustained blood pressure of 130 systolic and 80 diastolic, which again shows close approximation after the procedure is completed.

Case 12.—Mr. L. L., aged 41 and weighing 175 pounds (80 Kg.), had hypertensive vascular disease with headaches. On his admission to the hospital the blood pressure (March 17, 1947) was 202 systolic and 140 diastolic, and with an "etamon chloride" test on March 25 it dropped from 180 systolic and 120 diastolic to 108 and 60. The first stage operation was done on March 31 and the second stage on April 24. The fact that there was extreme lability of the blood vessels indicated a warning signal that the extent of the second stage operation should be limited. The blood pressure on his discharge from the hospital was 130 systolic and 90 diastolic This case was interesting in that the blood vessels were extremely labile as demonstrated by the "etamon chloride" test and that since he returned home he has had considerable discomfort from hypotension. In November 1947 the blood pressure was 130 systolic and 90 diastolic. Because the patient was depressed he was referred to a psychiatrist.

Case 13.—Mr. W. B. B., aged 48 and weighing 150 pounds (68 Kg.), had hypertensive vascular disease of group 3, with three previous hemorrhages. On his admission to the hospital the blood pressure (March 26, 1947) was 210 systolic and 90 diastolic, and on April 3 after an "etamon chloride" test it came down from 200 systolic and 120 diastolic to 145 and 105. The administration of "sodium amytal" reduced the blood pressure from 200 systolic and 110 diastolic to 120 and 90. The first stage operation was done on April 8 and the second stage on May 1. After the first stage the blood pressure became stabilized at about 180 systolic and 120 diastolic. Because he did not react well on the table during the second stage, a profound drop in pressure occurring while he was under the anesthetic, section of nerves was not carried out. He was allowed to go home, with the understanding that section would subsequently be performed. He had a paroxysmal hyper-

tension (280 systolic and 200 diastolic). After an incomplete second stage operation was performed the pressure became stabilized again at about 120 systolic and 110 diastolic, and he felt well. Paroxysmal hypertension subsequently developed, and he died.

### OPERATIVE PROCEDURE

The operative procedure is carried out in two stages. The first stage consists in radical splanchnicectomy and sympathectomy performed on the right side. The greater, lesser and least splanchnic nerves from the fourth thoracic ganglion are removed, and the greater splanchnic nerve proximal to the semilunar ganglion and the sympathetic chain from the fifth dorsal to the third lumbar ganglion are divided. Removal of the lumbar ganglion tips the balance between a good and a doubtful result. The first stage is recommended for the right side not because of anatomic or physiologic difference between the right and left sides but purely from a mechanical angle for the convenience of a right-handed operator. Mechanically it takes longer, and therefore it makes the second stage, in which the duration of anesthesia is more important, more easy and less time consuming.

The second stage is carried out at the completion of the reactionary rise in the blood pressure. This may occur as soon as fourteen days after the first stage or may require one hundred and twenty days, according to the age of the patient. The lapse of time between the first and the second stage allows the patient adequate time to compensate for the first drop in systolic and diastolic pressure (280 systolic and 130 diastolic to 180 and 110). The second stage is necessary to prevent the blood pressure from rising gradually to preoperative levels in six to eight months. Great care has to be exercised in the second stage of the operation or otherwise the blood pressure will fall beyond control to the extent that the patient will be lost on the operating table. In some cases the second stage is just as radical as the first, in others only two rami are divided and in others section of nerves is abandoned. The extent of resection in the second stage is based on the systolic and diastolic pressure when stabilized after the first stage, i. e., the response of the blood pressure to the anesthetic, to exploration of the kidneys, to blocking of the greater and lesser splanchnic nerves with 2 per cent procaine hydrochloride and to blocking of the dorsal sympathetic chain.

### TECHNIC OF OPERATION

The hypertensive patient is given at least three days of rest in bed prior to operation in order to lower the ceiling level. On the evening preceding operation 3 grains (0.19 Gm.) of pentobarbital sodium is given to support the ceiling level of the blood pressure; forty-five minutes before operation 1.2 grains (0.072 Gm.) of pentobarbital sodium and 0.006 grains (0.00036 Gm.) of atropine sulfate are given.

The patient is then intubated on the operating room carrier and transferred to the operating table, which has been fitted with special mattresses placed 4 inches (10 cm.) on each side of a central hinge. The patient faces downward, so that there is no support of the lower half of the chest or of the abdominal wall. The forearms and hands are supported on a special rest, so that the shoulders are abducted. The patient is then strapped to the table in such a way as to prevent sliding when the operating table is broken or tilted. The anesthetist records the systolic and diastolic blood pressure before starting the induction, after the induction and when the patient is finally in the correct posture. The anesthetic is for the greater part cyclopropane,

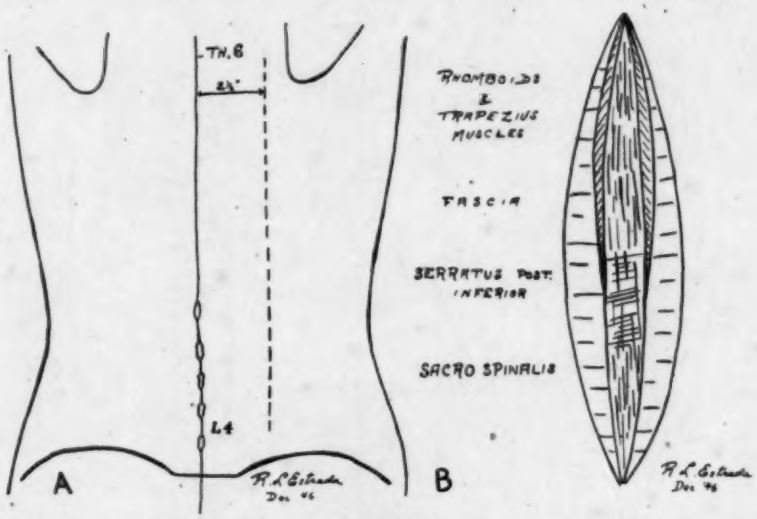


Fig. 1.—*A*, the vertical incision of the skin (instead of an incision curving in the direction of the iliac crest, which caused necrosis of the skin); *B*, the exposure of the sacrospinalis muscle by division of the fascia at the lower part of incision and then the serratus posticus inferior, trapezius and rhomboid muscles proximally. The fascia and muscles are then retracted laterally to expose the lateral border of the sacrospinalis so that it may be retracted medially instead of splitting the muscle fibers.

given intratracheally, but ether is periodically added to increase the blood pressure if necessary.

Before the preparation is applied to the skin the table is broken in order to flatten out the lumbar curve, which gives the operator a flat surface on which to work.

The incision is made 3 to 4 inches (7.6 to 10 cm.) to the right of the midline from the sacroiliac joint to the sixth thoracic vertebra. The fascia in the lower third of the wound is incised parallel to the incision in the skin and this incision extended downward to the level of the

fourth lumbar vertebra and then upward, dividing the serratus posticus inferior, the trapezius and the rhomboid muscles up to the level of the sixth dorsal vertebra. This procedure exposes the sacrospinalis muscle group, which is not split but reflected to the midline to expose the lower five ribs and the lumbodorsal fascia below the twelfth rib.

The lumbodorsal fascia is then divided from the twelfth rib to the level of the fourth lumbar vertebra, which exposes the quadratus lumborum muscle, also reflected to the midline. The first lumbar nerve comes into view. The median 3 inches (7.6 cm.) of the first lumbar nerve is then resected.

The renal space behind the peritoneum has now been exposed. The peritoneum is then stripped off the psoas major muscle, which exposes

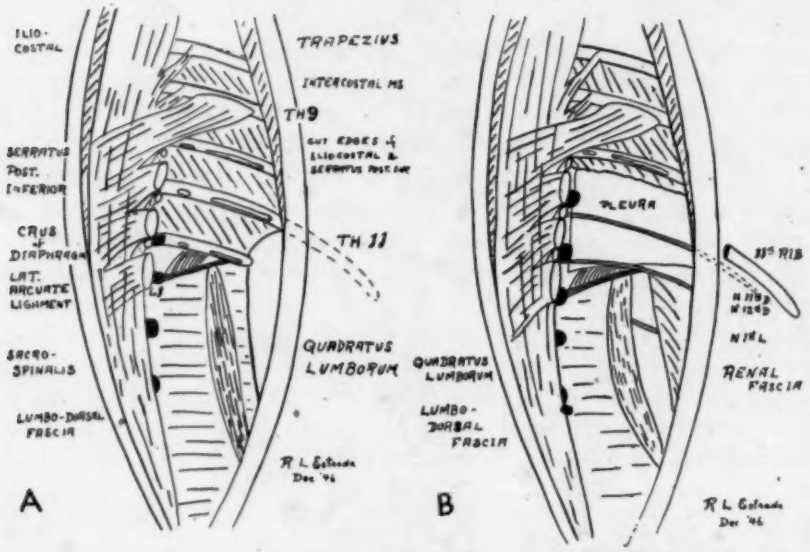


Fig. 2.—*A*, exposure of lower three ribs, crus and diaphragm and quadratus lumborium muscle below the divided lumbodorsal fascia. *B*, exposure of pleura by resection of the eleventh and twelfth ribs, with the eleventh and twelfth subcostal nerves lying on the pleura and the first lumbar nerve lying on the posterior aspect of the peritoneum. The tenth rib is now usually resected also, which bares the tenth subcostal nerve.

the inferior vena cava and the first, second and third lumbar vertebral bodies. The kidney is then carefully examined for size and abnormality, and the capsule is stripped in order that the cortex may be examined. A biopsy of the renal cortex is not usually made.[5] An adrenal medullary tumor is then searched for. The presence of an atrophic kidney indi-

5. Castleman, B., and Smithwick, R. H.: The Relation of Vascular Disease to the Hypertensive State Based on a Study of Renal Biopsies from One Hundred Hypertensive Patients, J. A. M. A. **121**:1256-1261 (April 17) 1943.

cates the necessity of performing nephrectomy rather than of proceeding with sympathectomy.[6] A small granular kidney suggests that sympathectomy will give disastrous results, such as anuria and uremia resulting in death. An adrenal medullary tumor (pheochromocytomas) is

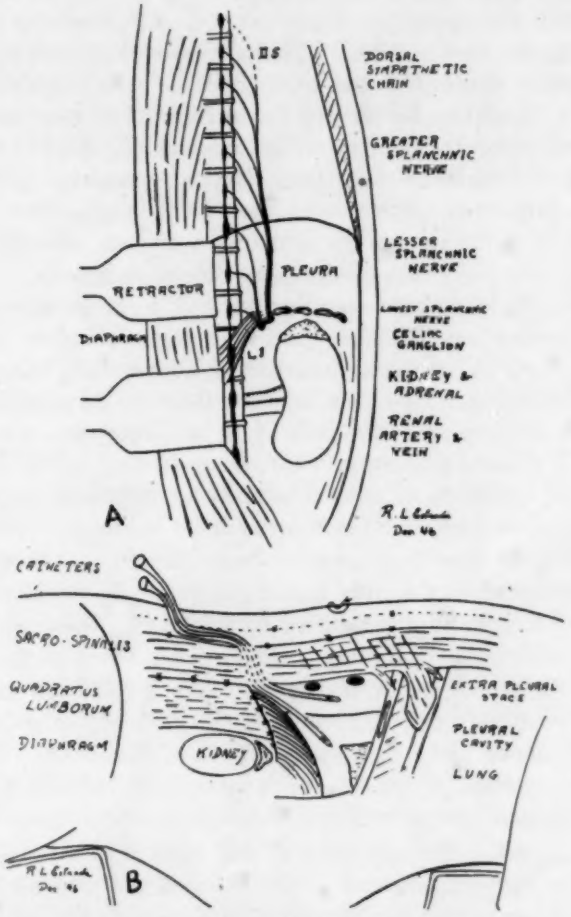


Fig. 3.—*A*, the retropleural and retroperitoneal spaces have been combined to form one cavity by dividing the crus of the diaphragm. The structures under investigation are the splanchnic nerves, the thoracic and lumbar sympathetic chain and the kidney and adrenal. *B*, the closure of wound in layers from below upward to the surface, with catheters in place for the aspiration of residual air in the pleural and retropleural spaces.

usually associated with paroxysmal hypertension; if found it should be resected and the idea of sympathectomy should be abandoned. If there

6. Goldblatt, H.: The Renal Origin of Hypertension, Physiol. Rev. **27**:120-165, 1947.

are no contraindications to sympathectomy, the lumbar sympathetic chain is isolated and the peritoneum stripped off the crus of the diaphragm.

The thoracic cavity is then opened by resecting the twelfth rib and 3 inches (7.6 cm.) of the eleventh and tenth ribs subperiosteally. In order to limit postoperative discomfort the tenth, eleventh and twelfth intercostal nerves are resected. The corresponding intercostal arteries and veins are doubly ligated and divided. The intercostal muscle bundles are divided and pulled to the midline to be used as retractors. The parietal pleura is then carefully stripped off the vertebral bodies from the diaphragm to the fourth dorsal vertebra. If the pleura is torn, a large rent is made to prevent the annoyance of a flapping pleura. The crus of the diaphragm is then divided to expose the twelfth dorsal and first lumbar sympathetic ganglions. The greater and lesser splanchnic nerves are then located. The former can usually be located about 1 or 2 inches (2.5 to 5 cm.) lateral to the midline, lying on the pleural reflection, just above the diaphragm, but occasionally it is found running in the cleft between the vena cava and the aorta. The blood pressure and the pulse rate are recorded, and then the greater and lesser splanchnic vessels are blocked with 2 per cent procaine hydrochloride to cut off splanchnic impulses and produce a gradual depression of the blood pressure. While the fall in blood pressure is being awaited, the sympathetic chain is isolated from below the second lumbar to the fifth dorsal ganglion. If the blood pressure falls below 120 systolic it is boosted by 0.5 cc. of phenylephrine hydrochloride intramuscularly; if there is no response, 0.5 cc. of phenylephrine hydrochloride and 3 cc. of nikethamide are given intravenously. If there is a satisfactory response, the greater and lesser splanchnic nerves are cut just above their respective ganglions. However, if there is no response the section of the nerves is postponed for half an hour; if there is still no response after that the operation is discontinued and the wound closed. The indication is that because of myocardial weakness the blood pressure cannot be sustained in the presence of pressor substances acting on the capillary bed. "Always divide splanchnic and sympathetic nerves on a rising blood pressure otherwise the blood pressure will fall beyond control."

The splanchnic nerves (lesser and greater) are then dissected from below up to the level of the fourth or fifth dorsal nerve, the branches being clipped before the division. Clips prevent bleeding from associated vessels and possibly regeneration of sympathetic vessels, though the latter is somewhat doubtful. I do not believe that sympathetic nerves regenerate, but associated fibers not interfered with possibly are subject to hypertrophy.

If the blood pressure shows a fall, phenylephrine hydrochloride is again used, and when it rises the sympathetic chain in the region of the eighth, ninth, tenth and eleventh nerves is blocked with 2 per cent procaine hydrochloride. After a satisfactory rise the lumbar chain is clipped and divided just above the fourth lumbar ganglion. The white rami are then clipped and divided from below up to the fifth thoracic ganglion, providing the blood pressure can be maintained, and the chain clipped and divided at this level. Care should be taken at the ninth thoracic ramus; possibly this should be doubly clipped to prevent hemorrhage from an unusually large vessel since it is hard to locate if bleeding occurs. The amount of sympathetic chain resected must be determined by the fall of the blood pressure and by the response to pressor drugs.

Closure of the wound is done in stages, no. 24 cotton and no. 10 cotton sutures being used. The diaphragm and the lumbodorsal fascia are reunited with interrupted cotton sutures. No attempt is made to repair the rent in the pleura if such has occurred, but a no. 18 rubber catheter is placed in the pleural cavity and a similar one in the extrapleural space above the tear. These catheters are passed between fibers of the sacrospinalis muscle at the lower end of the wound. The sacrospinalis muscle is then loosely tacked back in position. The sheath and the serratus posticus inferior trapezius and rhomboid muscles are then reunited with no. 10 cotton to enclose the sacrospinalis muscle. A series of interrupted cotton sutures are used to unite the subcutaneous fascia and the skin. The vertical mattress type of suture is used for the skin.

The lung is expanded by forcing oxygen and compressing the rebreathing bag. Both catheters are then clamped with Kelly forceps, and a large asepto syringe is attached to the catheter in the pleural space for the aspiration of any residual air. While aspiration is being carried out the catheter is withdrawn and the extrapleural catheter is treated in a similar manner. If there has not been a pleural tear, only the latter catheter is used in order to ensure collapse of extrapleural space and so prevent an extrapleural effusion, which may occur and cause delay in the convalescence.

The final procedure on the part of the anesthetist is to administer 0.5 cc. of phenylephrine hydrochloride and 3 cc. of nikethamide while the skin is being closed unless the blood pressure is 180 systolic. This prevents a fall in blood pressure during transportation of the patient from the operating table to the ward. Moving should be done carefully and gradually; otherwise the blood pressure will suddenly fall.

During the procedure, fluids in the form of isotonic solution of sodium chloride, blood or plasma are dispensed with. This results in

less sweating and less cardiac embarrassment. The fluid loss is minimal, but capillary dilatation is maximal, warranting the support of capillary circulation by the use of pressor drugs.

### POSTOPERATIVE ROUTINE

The postoperative procedure is as follows: On his return from the operating room the patient is kept flat, with a small pillow under the head. Under no consideration should the foot of the bed be elevated. To compensate for the lumbar curve and relax the abdominal muscles, the patient may be put in a low Fowler position after eight hours if the condition warrants it.

The blood pressure is checked every fifteen minutes for forty-eight to seventy-two hours and then every half hour for twenty-four hours. If the blood pressure is found to be stabilizing at a level of over 120 systolic without the use of pressor drugs, the intervals between readings may be prolonged, but the pressure should be determined at least twice a day up until the eighth or ninth postoperative day. The pressure should be maintained at about 120 mm. of mercury by the use of pressor drugs such as 0.5 cc. of phenylephrine hydrochloride repeated as often as every fifteen minutes and supported by the administration of 1 liter of plasma. My colleagues and I have found, as a rule, that unless there is a failing myocardium the phenylephrine hydrochloride is sufficient. We have given up using blood or plasma during the operation.

If the patient is not voiding, catheterization should be carried out every eight hours and the quantity of urine noted in order to be on the lookout for anuria. On no account should the blood pressure be allowed to fall below 80 mm. of mercury, since that is the normal filtration pressure of the kidneys.[7] The patients are allowed to have fluids and are allowed to eat as soon as they desire food. As a rule they are kept in bed for five to seven days after operation, although in some cases they get up on the third day. This prolonged rest in bed is not on account of the wound but is to prevent a hypostatic drop in blood pressure, with blackout. The routine for the second stage operation is the same as that for the first with the exception that the period in bed is prolonged by about one week.

We have found vitamin K (10 mg. daily for ten days supported by 200 mg. of vitamin C) to be of some advantage in preventing an extrapleural effusion.

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7. Goldring, W.; Chassis, H.; Ranges, H. A., and Smith, H. W.: Effective Renal Blood Flow in Subjects with Essential Hypertension, J. Clin. Investigation **20**:637-653, 1941.

### IMMEDIATE AND REMOTE COMPLICATIONS

The immediate complication may be considered as renal failure due to a drop in the filtration pressure in the kidneys and resulting in anuria, uremia and death. It is more frequently seen in cases in group 4. In cases belonging to group 4 in which there has been a history of anginal pain a coronary infarct is liable to develop. Patients with a poor myocardium are subject to a myocardial breakdown. Patients in whom it has been found difficult to maintain a systolic blood pressure of 120 by the use of either pressor drugs or plasma are subject to a pontile shutdown, which produces high fever, pinpoint pupils and flaccid paralysis.

We have had 1 case of paraplegia following shutdown and thrombosis of the anterior spinal artery. I believe that in nearly every clinic in which hypertension is treated by the operative procedure this complication has been encountered.

It has been our experience to encounter an occasional instance of extrapleural effusion, necessitating aspiration, about seven to ten days postoperatively, when the blood pressure is becoming stabilized. In the presence of an extrapleural effusion there is always the possibility of an extrapleural infection which has to be treated by open drainage. We have had few instances of pleural effusion associated with a pleural tear. The majority occur when there has not been a pleural tear, and we are led to believe that the extrapleural effusion can be prevented by the administration of vitamin K immediately after operation.

The remote complication may be considered as a vascular shutdown, which occurs after about six to seven days, resulting in anuria, uremia and death. Hypotension or blackouts on arising in the morning have not been experienced by our patients except when thyroidectomy for hypertension has previously been performed. However, the hypotension can be controlled by action and by the use of corsets and bandages.

Pain of a toothache-like and girdle type frequently exists along the ribs and over the great trochanter. Resection of the tenth, eleventh and twelfth spinal nerves and of the first lumbar nerve will prevent a great deal of this discomfort. A part of it is possibly postural since the patients have much less pain after undergoing the second stage of the operation; all have some pain and discomfort for six months postoperatively.

Most patients are subject to what I consider a lackadaisical depression, which can be helped by the administration of phenobarbital and an iron tonic and by cheery visitors. Hypertensive patients have to be ordered about after operation. The more they are made to look after themselves the better they progress.

We have had 2 cases of paradoxic hypertension following the second stage operation. We cannot account for this since there was no evi-

dence of an adrenal medullary tumor. The hypertension subsequently cleared up, but the patients died within six months.

## SUMMARY

The selection of cases for surgical treatment of hypertension is important. Cases should be arbitrarily grouped as belonging to groups 1, 2, 3 and 4 and as cases of rapidly progressing hypertensive vascular disease. The various complications mentioned increase the risk. The risk is especially increased in regard to patients who have had albuminuria for a long period, anginal attacks or myocardial breakdown. Although the renal function has been carefully taken into consideration, the kidneys should be carefully examined before section of nerves is performed. Posture is most important in the mechanical phase of the operation. Furthermore, the foot of the bed should not be elevated to increase the blood pressure since paraplegia may occur, and the pressure should be controlled by the use of pressor drugs rather than blood in the operating room. Nerve block will control the fall in blood pressure and will give the operator some indication as to the extent of resection to be carried out.

The use of vitamin K has been suggested to control postoperative serous effusion. There should be sufficient time between the first and second stages to allow of compensation for the first mechanical lowering of the blood pressure. There may be renal failure as late as five to six days postoperatively. Pressor drugs have not seemed to be of much avail in myocardial breakdown or in anginal attacks; even plasma is not of much importance. Patients with these complications usually succumb after operation. One must bear in mind that in order to assess the value of the operation a year or more should be allowed to elapse, since accommodation to the procedure takes at least a year.

The discomfort of the girdle type usually disappears in about six months. The psychiatrist seems to be able to help the patients a great deal in their convalescence.

The use of tetraethylammonium chloride has been advised as the best means of estimating the postoperative results. Sixteen cases have been analyzed, 3 of which are not included in the reports. From eight to eighteen months have elapsed since operation, and the blood pressure curves are satisfactory.

I have not made any reference as to how good results can be estimated but would suggest that they be assessed on the basis of relief of symptoms, the approach to normal of the systolic and diastolic pressure, improvement in the eye signs, improvement in the electrocardiogram and improvement in the renal function.

NOTE.—Special reference was made, during the operative procedure, to maintenance of systolic blood pressure by the use of pressor drugs,

i. e., 0.5 cc. of phenylephrine hydrochloride associated with limitation of whole blood or plasma. Some changes have been introduced during the lapse of time since this article was submitted for publication which give a more uniform and rapid control of blood pressure as a supplement. Two Baxter bottles, each of 500 cc. capacity, one containing isotonic saline solution and the other a 5 per cent solution of dextrose in isotonic saline solution, are arranged for infravenous administration with a Y connection as close as possible to the intravenous needle. Phenylephrine hydrochloride, 5 cc., is injected into the 5 per cent dextrose and isotonic saline solution bottle and agitated for dispersion. The isotonic saline solution is used only to keep the needle from blocking and therefore is allowed to run only sufficiently fast to maintain patency of the needle. When fall in blood pressure warrants the pressor drug, the bottle with saline solution is clamped, then the dextrose-saline-phenylephrine solution is allowed to flow about 30 drops per minute and the rate reduced according to the blood pressure response to maintain a constant systolic pressure of about 120 mm. of mercury. A rapid fall in blood pressure may require in addition 0.5 cc. of phenylephrine hydrochloride to be given intramuscularly or intravenously.

Further, this procedure is frequently used for the first six to eight hours after operation, more especially on account of scarcity of nursing care.

## DISCUSSION

DR. AUGUST F. JONAS JR., Erie, Pa.: In relation to the paper of Dr. Pretty on hypertension, one of the complications which we have noticed after surgical treatment is a persistent and severe intercostal neuralgia. Dr. Pretty divides the intercostal nerve. I should like to ask if this completely obviates the neuralgia and whether he has had any troublesome bulge of the rectus muscle after this procedure.

DR. H. GURTH PRETTY, Montreal, Canada: That remark by Dr. Jonas is well taken. I find that resection of the eleventh and twelfth nerves and sometimes the tenth does obviate about 80 per cent of the neuralgia but that it does not obviate the neuralgia entirely. The bulge of the rectus muscle disturbs the patient a little until after the other side has been operated on. After that it seems to be compensated. Incidentally, it is interesting to note that this neuralgia after resection of the nerves is not of any great importance. Patients will complain of pain and the distribution of the pain after operation on the right side has been performed. After the left side has been operated on they will tell you that the right side is entirely free of pain. If the neuralgia was of any great importance, they would feel it. They will tell you that all the pain is gone from the right side because they are concentrating on the second stage. So obviously it is of no consequence.

I find that there is a distinct advantage in not using blood or plasma while the patients are on the operating table. The last 15 or 20 patients have had no transfusions, plasma or intravenous injections of sodium chloride. We notice that when they get blood while they are on the table they tend to perspire and lose salts and they go back to the room in relative shock. The blood is not being lost but merely displaced into larger space, and we get better results by controlling the carriers than by adding excess fluids.

# TREATMENT OF PEPTIC ULCER WITH ENTEROGASTRONE

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THE OBJECT of this report is to present a preliminary survey of our clinical and laboratory observations on the use of enterogastrone in the treatment of peptic ulcer as well as on its physiologic effects in man. Previous reports [1] on the use of this substance in man have attempted to evaluate its therapeutic effectiveness largely on the basis of a comparison of the recurrence rate of duodenal or gastric ulcer before and after treatment with enterogastrone. Thus Greengard and his co-workers [1b] believed that their therapeutic trial of enterogastrone on 58 patients suffering from peptic ulcer over a period of years had demonstrated the probability that the drug is effective in preventing recurrences during the period of its administration and for a length of time thereafter as yet undetermined. No explanation of the action of enterogastrone was reported, but the opinion was expressed that possibly it increases the resistance of the upper digestive tract, as previously suggested by Sandweiss.[2]

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From the Department of Internal Medicine, University Hospital, University of Michigan, aided by a grant from the United States Public Health Service.

The enterogastrone for oral administration was supplied by the Abbott Laboratories. The enterogastrone given parenterally was supplied by the Upjohn Company.

Read in a Symposium on Peptic Ulcer at the joint meeting of the Section on Gastro-Enterology and Proctology and the Section on Surgery, General and Abdominal, at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, June 19, 1947.

1. (*a*) Ivy, A. C.: Prevention of Recurrence of "Peptic" Ulcer; Experimental Study, Gastroenterology **3**:443 (Dec.) 1944. (*b*) Greengard, H.; Atkinson, A. J.; Grossman, M. I., and Ivy, A. C.: The Effectiveness of Parenterally Administered "Enterogastrone" in the Prophylaxis of Recurrences of Experimental and Clinical Peptic Ulcer, ibid. **7**:625-649 (Dec.) 1946.

2. Sandweiss, D. J.: Immunizing Effect of Anti-Ulcer Factor in Normal Human Urine (Anthelone) Against Experimental Gastrojejunal (Peptic Ulcer) in Dogs, Gastroenterology **1**:965-969 (Oct.) 1943.

In experimentation on animals [3] it has been demonstrated that enterogastrone protects Mann-Williamson dogs against postoperative jejunal ulcers. This type of ulcer developed in 98 per cent of the untreated animals, but when animals were treated with daily parenteral injections of enterogastrone for one year jejunal ulceration developed in only 21 per cent. The protective mechanism involved is obscure, but it has been demonstrated [4] that after administration of enterogastrone the hypersecretory pattern in a Mann-Williamson dog reverts to normal as demonstrated by an alcohol test meal.

The purpose of this study was to reinvestigate the purported effectiveness of enterogastrone in preventing the recurrence of peptic ulcer in man and, if recurrences were prevented, to investigate any measurable change in secretory or motor activities of the stomach that would aid in explaining the mechanism of protection. In addition, because previous clinical studies have reported results only with the parenteral use of enterogastrone it was considered desirable to compare the effect of the oral administration with that of parenteral administration. In order to accomplish these ends 28 patients with peptic ulcer were carefully studied before and during therapy with enterogastrone from the following aspects: (1) clinical response, particularly with regard to recurrences, (2) roentgenologic changes and (3) changes in gastric secretion and motility.

## METHODS OF STUDY

The following laboratory studies were carried out on all patients both prior to therapy and at frequent intervals during it. In most instances all control studies were repeated on several occasions.

1. Complete series of gastrointestinal roentgenograms, including studies of the upper gastrointestinal tract, cholecystographic studies and studies after a barium enema, were obtained prior to treatment. The study of the upper gastrointestinal tract was repeated at least at three month intervals. More frequent roentgenograms were obtained on patients with gastric ulcer and on those with duodenal ulcer in whom symptoms persisted or in whom there was clinical evidence of possible complications.

2. Gastroscopy was carried out in cases in which the symptoms suggested the possibility of an associated gastritis and in all cases of gatric ulcer in order better to assure ourselves that the lesion was benign.

3. The fasting continuous gastric secretion and motility were usually studied simultaneously. This was accomplished by the method illustrated in figure 1. A double-lumened tube was utilized, and continuous suction was applied to the proximal lumen. The aspirated secretion passed through a chamber holding a glass

3. (*a*) Hands, A. P.; Greengard, H.; Preston, F. W.; Funley, G. B., and Ivy, A. C.: Prevention of Experimental Gastrojejunal Ulcer by Enterogastrone Therapy, Endocrinology **30**:905-911 (June) 1942. (*b*) Ivy.[1a]

4. Grossman, M. I.; Greengard, H.; Dutton, D. F., and Woolley, J. R.: Effect of Prolonged Administration of Enterogastrone on Gastric Secretion in Normal and Mann-Williamson Dogs, Gastroenterology **2**:437-441 (June) 1944.

electrode, which together with a calomel electrode was connected to a $p_H$ meter. From here the secretion passed to a special drop recorder which recorded the number of drops on a kymograph. The volume of secretion and the $p_H$ were measured every fifteen minutes. In addition to this, peptic activity of the gastric juice was determined by the method of Anson and Mirsky.[5] A balloon was attached to the distal lumen of the tube. This was inflated with 10 cc. of air and through a water monometer recorded gastric motility on the kymograph. Each secretion-motility study was carried out for a period of three to six hours.

4. Caffeine fractional analyses were carried out according to the technic described by Roth and his co-workers.[6] Results were plotted as graphs indicating volume of secretion and output of hydrochloric acid.

## CLINICAL OBSERVATIONS

1. *General.*—The material comprising this study consists of 28 patients treated with enterogastrone, 16 parenterally and 12 by the

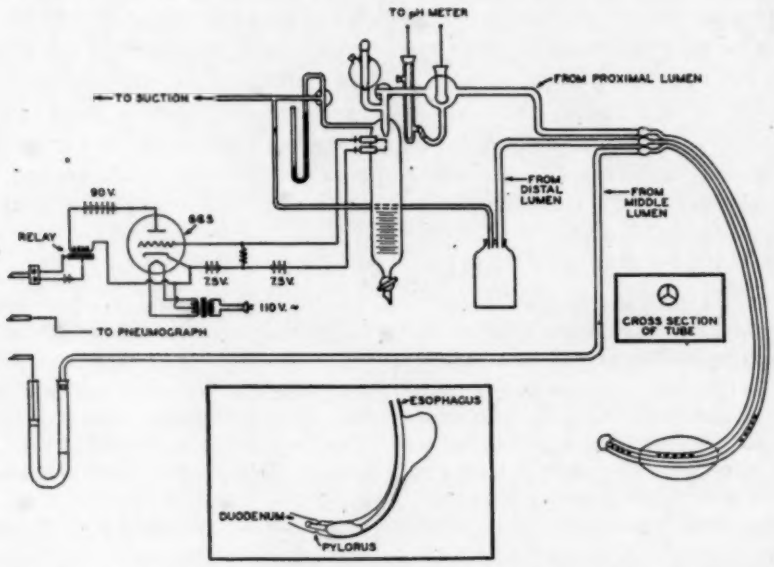


Fig. 1.—Arrangement for simultaneous study of gastric secretion and motility.

oral route (tables 1 and 2). For treatment were accepted only persons who had a long history of peptic ulcer, with at least two annual recurrences in the years preceding the present episode. In fact the majority of our patients had been referred to the hospital for surgical treatment, having been considered "medical failures." Most of the patients were

5. Anson, M. L., and Mirsky, A. E.: Estimation of Pepsin with Hemoglobin, J. Gen. Physiol. **16**:59-63 (Sept.) 1932.

6. Roth, J. A.; Ivy, A. C., and Atkinson, A. J.: Caffeine and "Peptic" Ulcer: Relation of Caffeine and Caffeine-Containing Beverages to the Pathogenesis, Diagnosis and Management of "Peptic" Ulcer, J. A. M. A. **126**:814-820 (Nov. 25) 1944.

on some type of bland diet and antacid preparation at the time treatment with enterogastrone was started. All patients continued on a modified Meulengracht diet and were given an aluminum or mag-

TABLE 1.—*Clinical Data on Twelve Patients with Peptic Ulceration Treated With Enterogastrone*

| Case | Sex | Age | Diagnosis | Duration of Symptoms, Yr. | Duration of Therapy, Mo. | Clinical Course |
|---|---|---|---|---|---|---|
| 1 | M | 42 | Duodenal bulb deformity | 16 | 8 | Asymptomatic |
| 2 | M | 33 | Duodenal bulb deformity | 10 | 11 | One recurrence at 10 months |
| 3 | M | 49 | Duodenal ulcer crater | 17 | 11 | Asymptomatic |
| 4 | M | 46 | Duodenal ulcer crater | 21 | 6 | Severe recurrence; vagotomy |
| 5 | M | 48 | Duodenal ulcer crater | 10 | 7 | Asymptomatic |
| 6 | M | 40 | Gastric ulcer | 11 | 6 | No symptoms |
| 8 | M | 47 | Duodenal bulb deformity | 15 | 5 | Asymptomatic |
| 23 | F | 30 | Duodenal bulb deformity | 6 | 1 | Asymptomatic |
| 24 | M | 58 | Duodenal bulb deformity | 5 | ¾ | Asymptomatic |
| 25 | M | 48 | Duodenal bulb deformity | 8 | ¾ | Asymptomatic |
| 26 | M | 30 | Duodenal bulb deformity | 6 | ¾ | Asymptomatic |
| 28 | M | 37 | Duodenal bulb deformity | 12 | ½ | Asymptomatic |

TABLE 2.—*Clinical Data on Sixteen Patients With Peptic Ulceration Given Enterogastrone Intramuscularly*

| Case | Sex | Age | Diagnosis | Duration of Symptoms, Yr. | Duration of Therapy, Mo. | Clinical Course |
|---|---|---|---|---|---|---|
| 7 | M | 49 | Duodenal bulb deformity | 20 | 5 | Asymptomatic |
| 9 | M | 62 | Duodenal bulb deformity | 15 | 9 | Asymptomatic |
| 10 | M | 54 | Duodenal bulb deformity | 18 | 1½ | Asymptomatic; use of drug discontinued because of allergy |
| 11 | M | 44 | Jejunal ulcer | 9 | 5 | Asymptomatic |
| 12 | M | 45 | Duodenal bulb deformity, with 90% retention | 23 | ¾ | No relief; surgical treatment |
| 13 | M | 64 | Duodenal bulb deformity | 15 | 3½ | No change in symptoms; vagotomy |
| 14 | M | 50 | Duodenal ulcer crater, with 50% retention | 10 | 4½ | Asymptomatic |
| 15 | M | 53 | Gastric ulcer and duodenal bulb deformity | 8 | 4 | Asymptomatic |
| 16 | M | 57 | Duodenal bulb deformity | 6 | 3 | Unable to tolerate parenteral administration of drug and given it orally; asymptomatic |
| 17 | M | 43 | Duodenal bulb deformity | 12 | 2½ | Asymptomatic |
| 18 | F | 53 | Duodenal ulcer crater | 9 | 2½ | Asymptomatic |
| 19 | M | 50 | Duodenal bulb deformity | 17 | 2½ | Asymptomatic |
| 20 | M | 34 | Duodenal ulcer crater | 21 | 2 | Asymptomatic |
| 21 | M | 40 | Gastric ulcer and duodenal bulb deformity | 15 | 2 | Symptoms persist |
| 22 | M | 41 | Duodenal bulb deformity | 15 | ¾ | Asymptomatic |
| 27 | M | 40 | Duodenal bulb deformity | 20 | ½ | Asymptomatic |

nesium preparation and belladonna. This regimen was gradually abandoned during the first thirty to sixty days of enterogastrone therapy.

2. *Dosage.*—This had to be largely empiric because the possible effectiveness of enterogastrone in human beings and the mode of action are both unknown. When orally administered, the drug was given in doses ranging from 8 to 16 Gm. daily. When parenterally administered,

200 mg. was given daily for six days of each week. This dosage was based to some extent on the fact that a daily dose of 100 mg. given parenterally was effective in preventing jejunal ulcers in Mann-Williamson dogs.[3] However, it is certainly questionable whether this dosage scale can be so simply applied to cases of peptic ulcer in human beings.

3. *Reactions to Enterogastrone.*—The preparation for oral use was at no time observed to cause any discomfort or disturbance. The preparation given intramuscularly caused definite local tenderness and discomfort in most cases but usually only in association with the first few injections. The discomfort at the site of injection usually lasted for several hours. After a week or two these local reactions generally did not occur.

General reactions were reported in 4 instances, 2 of which might be considered questionable. In these 2 instances (cases 7 and 19) the patients reported that chills and fever developed after an injection. Subsequent injections made in this clinic did not evoke systemic changes, and it seemed possible that an infection of the upper respiratory tract was present at the time of the alleged reactions. In neither case was it necessary to discontinue the use of the drug, since no further chills or fever occurred. The patient in case 10, who had severe asthma, had progressively increasing headaches from the first injection on. Cutaneous tests revealed that he was markedly sensitive to pork, and the reaction of his skin to intradermal injections of enterogastrone was more extensive and more prolonged than it was in the controls. Concomitant oral administration of tripelennamide hydrochloride (150 mg. daily) prevented further reactions to enterogastrone until hemorrhagic sinusitis subsequently developed. At this time it was deemed advisable to stop the treatment. One other patient (case 16) reported general malaise associated with the parenteral admininstration of the drug and in addition felt that the daily intramuscular injection was too much of an "ordeal," so that the preparation for oral use was substituted in this case. In summary, it was necessary to discontinue parenteral injection of enterogastrone in 2 of 16 patients because of marked sensitivity in one instance and in the other because the daily injection was too much of an ordeal.

4. *Summary of Clinical Effectiveness of Enterogastrone.*—Tables 1 and 2 summarize the clinical data on our group of treated patients and indicate the response to therapy. It will be noted that only 7 patients of our group (cases 1 to 6 and case 9) have been under treatment for six months or longer. Since the patients were selected on the basis of a history of two previous annual recurrences, we can evaluate the results of enterogastrone therapy on the recurrence rate only in these 7. Six of the patients were treated with oral injections of enterogastrone in

doses ranging from 8 to 16 Gm. daily. In cases 2 and 4 a typical recurrence was manifested in the tenth and sixth months of treatment respectively. In case 6 relief of the symptoms was gradually obtained and the gastric ulcer completely healed although slowly. However, in this particular case a definite social problem was present as well as many severe psychogenic factors so that relief of the symptoms was rather promptly followed by other complaints. In summary, 4 of 6 patients treated with oral injections of enterogastrone for six to eleven months obtained complete relief of symptoms and experienced a decrease in the incidence of recurrence.

In the case of duodenal ulcer in which the patient was treated for nine months (case 9) with intramuscular injections of enterogastrone there was complete relief of symptoms and no evidence of recurrence.

Three patients have been under treatment for five to six months (cases 7, 8 and 11). The patient in case 7, with a duodenal ulcer, was at first given enterogastrone orally but later was given it intramuscularly because of a disturbance of the bowel that was thought to be possibly related to the oral use of the drug. He has had no recurrence since the start of therapy. The patient in case 8, given the drug orally, has been asymptomatic to date. The patient in case 11 had a jejunal ulcer that developed after a subtotal gastric resection was performed. He had severe chronic bleeding from this ulcer. After three weeks of hospitalization and daily intramuscular injections the bleeding ceased and all discomfort disappeared; he has remained asymptomatic.

Two patients (cases 14 and 15) have received enterogastrone for four to five months. Both patients were given intramuscular injections and have remained asymptomatic. One patient (case 13) treated for three and one-half months had a recurrence, and a vagotomy was performed. The patient in case 10 was treated for six weeks with intramuscular injections of enterogastrone, but the use of the drug had to be discontinued because of an allergic reaction. However this patient has had no recurrence of symptoms for the five months since treatment was stopped, so that even this six week period of therapy may have been beneficial. In case 12 pyloric obstruction was present at the time therapy was instituted, at which time it was not realized that this obstruction was organic scar tissue. The nature of the obstruction was later proved at operation. The data on this case certainly cannot be used in a test of the efficacy of enterogastrone, and it must be excluded from our series for this evaluation. The patients in cases 16 to 28 have been under treatment for three months or less. In all these cases, with one exception (case 21), the clinical response has been satisfactory. In this group the effect of therapy on the recurrence rate cannot be

evaluated. Most of them, however, had had the typical symptoms of ulcer in spite of the medical therapy outlined by the physicians who referred them. These symptoms in general disappeared, but the question of whether this is due to the beneficial effect of the enthusiasm and assurance associated with the use of a "new" drug or whether there is a specific effect of enterogastrone must await further evaluation.

In summary, of the 12 patients given the drug orally 2 have had typical recurrences; 5 of these 12 patients have been under observation for less than one month. Of the 16 patients treated intramuscularly, 1 had a typical recurrence, 1 with pyloric obstruction obtained no relief and 1 (case 21) had no relief of symptoms after two months of treatment. This gives a total of 3 patients to date who have not benefited from enterogastrone clinically.

TABLE 3.—*Roentgen Study of Twenty-Eight Patients With Peptic Ulcer Treated With Enterogastrone*

| | Before Therapy | | After Therapy | | |
|---|---|---|---|---|---|
| | Follow-Up Available | No Follow-Up | Improved | No Change | Worse * |
| Deformity of duodenal bulb..... | 9 | 10 | .. | 6 | 3 |
| Duodenal ulcer crater..... | 3 | 2 | 2 | 1 | .. |
| Gastric ulcer..... | 2 | 1 | 2 | .. | .. |
| Jejunal ulcer..... | 1 | .. | 1 | .. | .. |
| Pyloric obstruction..... | 2 | .. | 1 | 1 | .. |
| Total..... | 17 | 13 | 6 | 8 | |

* Obstruction developed in 1 case (13), deformity became more marked in a second (16) and a crater developed in a third (21).

## ROENTGENOLOGIC OBSERVATIONS

Table 3 summarizes the roentgenologic appearance of the lesion in our series of 28 patients. It will be noted that a total of thirty roentgenologic diagnoses are listed for the 28. This disparity is due to the fact that in 2 patients (cases 12 and 21) both a gastric and a duodenal lesion were present. From table 3 it can be seen that in 17 cases follow-up roentgenograms have been obtained since treatment with enterogastrone was initiated. In 6 of these 17 there has been improvement in the roentgenologic appearance of the lesion. Improvement in the 6 cases consisted in the disappearance of a duodenal ulcer crater (cases 3 and 5), complete healing of a gastric ulcer as revealed by roentgenograms (cases 6 and 21), complete healing of a jejunal ulcer as seen in roentgenograms (case 11) and complete relief of previous pyloric obstruction (case 14). In 8 of the 17 cases there was no change in the roentgenograms. In 3 cases the roentgenologic appearance of the lesion was worse after therapy than before. In case 13 pyloric obstruction developed, in case 16 the deformity of the duodenal bulb was definitely

more severe and in case 21 a duodenal ulcer crater appeared. Case 21 is of special interest because initially a gastric ulcer and a duodenal deformity were present. After initiation of enterogastrone therapy the gastric ulcer healed completely and a crater appeared in the duodenum. Comparison with table 2 reveals that this change was associated with a persistence of symptoms.

The significance of the improvement in 6 cases in the roentgenologic appearance of the lesion is difficult to determine in an evaluation of the effectiveness of enterogastrone therapy. In case 11 the healing of the jejunal ulcer appears significant in view of previous prolonged attempts to heal it by other forms of medical therapy. The fact that this type of ulcer is most closely related to the jejunal ulcer produced in Mann-Williamson dogs and prevented by enterogastrone therapy

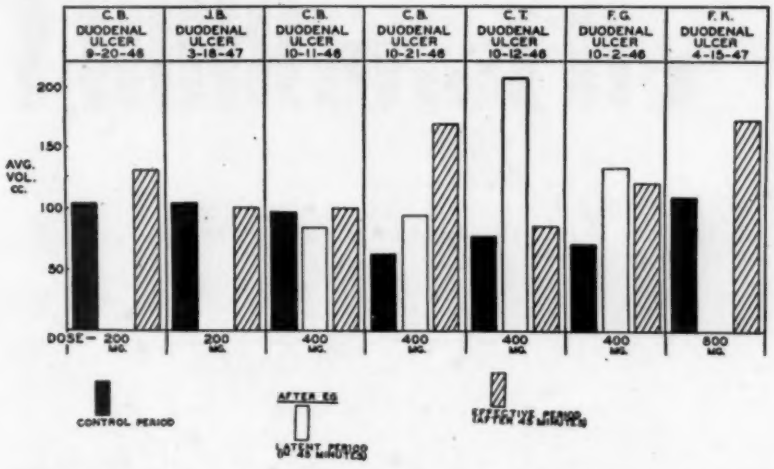


Fig. 2.—Effect of single intramuscular injection of enterogastrone on average hourly fasting volume of gastric contents.

may be important. One can hardly attribute the healing of the gastric ulcer in case 21 to enterogastrone in view of the fact that simultaneously a duodenal ulcer crater appeared.

In the 3 instances in which the roentgenologic appearance of the lesions was worse after enterogastrone therapy it can certainly be concluded that enterogastrone had no beneficial influence. It might be considered that the duration of therapy was not long enough in these instances to influence the source of the lesion. However, table 2 reveals that treatment in the 3 cases (13, 16 and 21) had been of three and one-half, three and two months' duration respectively. In the 8 cases in which there was no definite change in the roentgenologic appearance of the lesion the latter cannot be used as a criterion in the evaluation of

the influence of enterogastrone therapy. This is particularly true in view of the fact that 6 of the patients had initially a deformity of the duodenal bulb.

### LABORATORY FINDINGS

The effect of a single parenteral dose of enterogastrone on fasting gastric activity was studied in several cases. Figures 2, 3 and 4 show

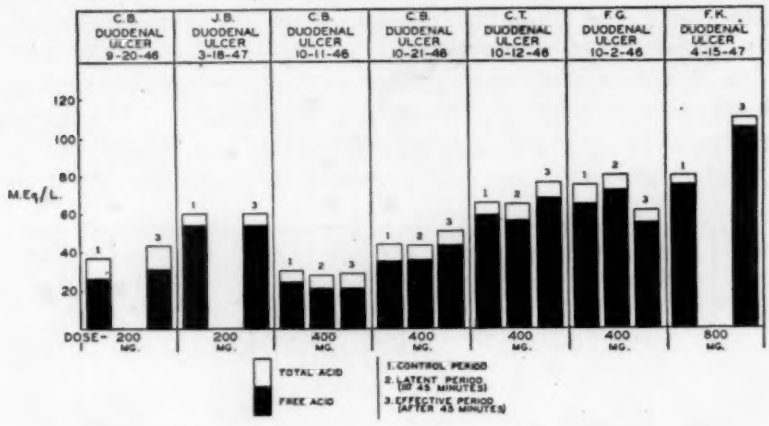


Fig. 3.—Effect of single intramuscular injection of enterogastrone on acidity of gastric contents.

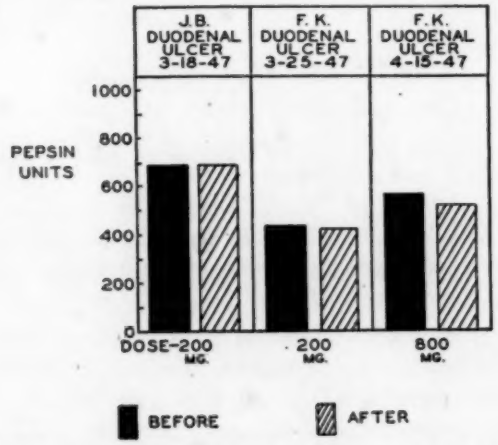


Fig. 4.—Effect of single intramuscular injection of enterogastrone on pepsin concentration.

that single injections of enterogastrone in amounts up to four times the daily clinical dose did not exert any inhibitory effect on the volume, acidity or pepsin concentration of the fasting gastric contents in patients

with peptic ulcer. The chloride content, both total and free, and the nonprotein and protein nitrogen contents were not significantly changed by a single intramuscular injection of 400 mg. of enterogastrone (table 4). Likewise, in each of these experiments enterogastrone had

TABLE 4.—*Effect of Parenteral Injection of Enterogastrone on Composition of Fasting Gastric Secretion in a Patient with a Duodenal Ulcer*

| | Average Hourly Volume, Cc. | $p_H$ | Free Acid: Average Hourly Output, Mg. M.Eq. | Free Acid: Average Hourly Output, Mg. HCl | Total Acid: Average Hourly Output, Mg. M.Eq. | Total Acid: Average Hourly Output, Mg. HCl | Chlorides, Mg./100 Cc. Free | Chlorides, Mg./100 Cc. Total | Nitrogen, Mg./100 Cc. Non-protein | Nitrogen, Mg./100 Cc. Protein | Nitrogen, Mg./100 Cc. Total |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Control period (3 hr. 15 min.)..... | 97 | 1.8 | 24 | 85 | 30 | 106 | 56 | 377 | 40 | 8 | 48 |
| After 400 mg. of enterogastrone | | | | | | | | | | | |
| Latent period (45 min.)..... | 84 | 1.7 | 21 | 65 | 27 | 81 | 47 | 291 | 33 | 4 | 37 |
| Effective period (1 hr. 15 min.)..... | 100 | 1.7 | 21 | 77 | 28 | 102 | 41 | 328 | 40 | 9 | 49 |

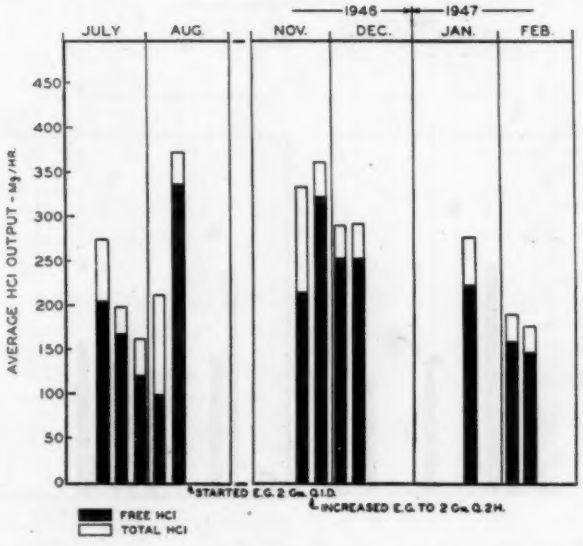


Fig. 5.—Cumulative influence of orally administered enterogastrone on gastric acidity in a patient with duodenal ulcer.

no effect on the motility of the fasting stomach as measured by the studies in which a balloon was used.

A study of the cumulative effects of enterogastrone on gastric acidity was also carried out. Figure 5 indicates that the average hourly

output of hydrochloric acid in the fasting state was not materially altered in a patient given enterogastrone orally over a considerable period. Figure 6 *A* shows that the same holds true for a patient given intramuscular injections. In addition, there was no evidence of alteration of the pepsin concentration in the same circumstances after prolonged daily oral (fig. 6 *B*) or intramuscular (fig. 6 *C*) administration. Figure

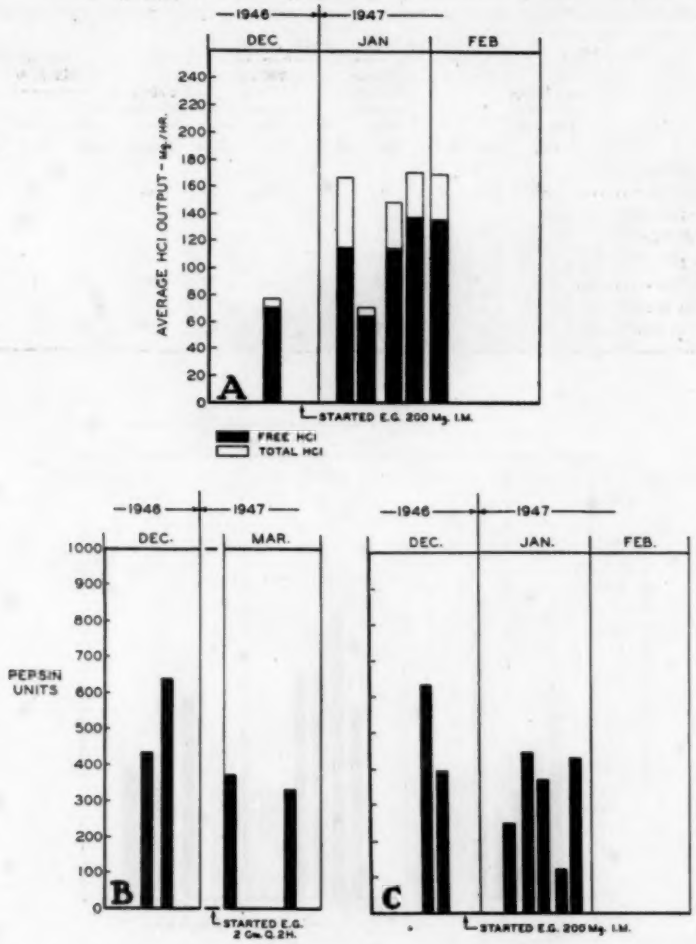


Fig. 6.—*A*, influence of daily intramuscular administration of enterogastrone on gastric acidity in a patient with a postoperative jejunal ulcer. *B*, influence of daily oral administration of enterogastrone on pepsin concentration of the gastric juice in a patient with duodenal ulcer. *C*, influence of daily intramuscular administration of enterogastrone on pepsin concentration of gastric juice in a patient with jejunal ulcer.

7 indicates that the type of secretory response to the caffeine test was not altered during periods of therapy extending up to ten months.

The findings illustrated in these figures were essentially characteristic of all our cases so that we were unable to demonstrate any significant alterations in output of hydrochloric acid, pepsin concentration and type of secretory response to caffeine as a result of the use of enterogastrone. This was true for both the oral and the parenteral administration and was likewise true whether there was clinical or roentgenologic evidence that ulceration remained stationary, improved or became worse.

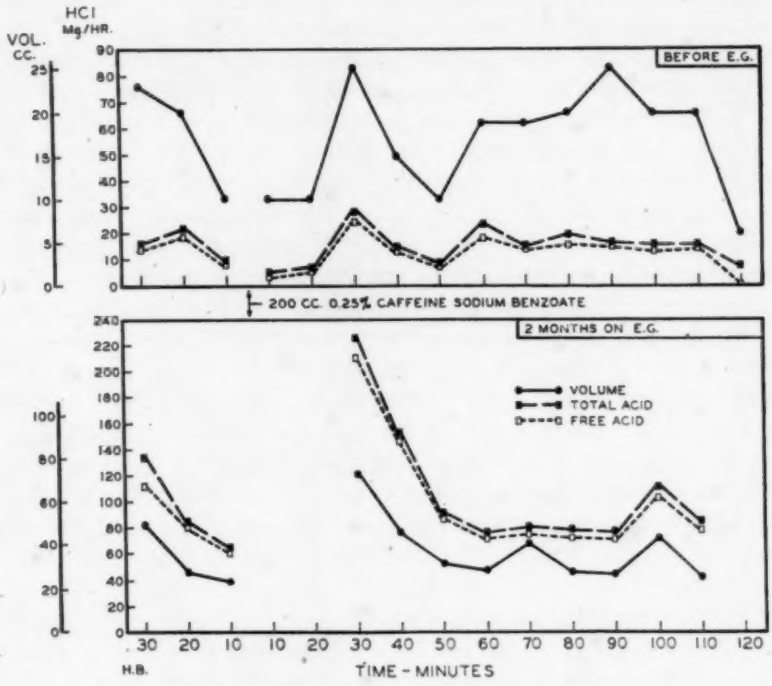


Fig. 7.—Effect of enterogastrone given parenterally on the response to a caffeine fractional test.

## COMMENT

Because of the small series of cases studied and because many of our cases have been observed for only a short period we do not feel that our clinical data is adequate for the establishment of any general conclusions with regard to the efficacy of enterogastrone in preventing or decreasing the incidence of recurrence of peptic ulcer. The fact that 2 of our patients given enterogastrone orally had recurrences after six and ten months of therapy may be of significance. Likewise, the failure to relieve symptoms or prevent recurrences in 3 of 16 patients given intramuscular injections of the preparation may indicate either

inadequate dosage, too short a period of therapy, inefficacy of the enterogastrone or selection of inappropriate types of cases (e. g., in case 12 there was pyloric obstruction) for such therapy. The deterioration in the roentgenologic appearance of the lesion in 3 of 17 cases has the same implications. The series is too small and the period of observation too short to decide which of these factors is important.

Our laboratory data are of more significance. Because the origin of peptic ulcer is generally related to abnormalities of gastric secretion (specifically acidity), gastric motility or both, it was felt that any specific therapeutic material for peptic ulcer in man might exert some influence on either or both of these abnormalities. Such an influence has been demonstrated in Mann-Williamson dogs.[3a] However all our data indicate that our preparation of enterogastrone in the dosage used either orally or intramuscularly and given daily up to eleven months does not influence gastric motility, volume of postabsorptive gastric secretions, gastric acidity or pepsin concentration of the gastric juice. Similar results were obtained with single intramuscular injections in amounts up to four times the daily therapeutic doses (800 mg.), These findings are of significance for two reasons. First, they indicate that, in man at least, if enterogastrone does exert any beneficial action on peptic ulcer it is through some mechanism other than its effect on gastric motility or gastric secretory activity. Secondly, they invalidate the utility of the study of gastric secretion and motility as an objective measure in following the response of peptic ulcer in persons under treatment with enterogastrone. These tentative conclusions can obviously apply only to the present preparations of the material and the present dosage scales. A future, more highly purified, material that can be given in larger doses may reveal a more favorable response. Because of the local reaction that occurs with the present preparation, we feel that the use of larger amounts either for a daily schedule or for a study of acute effects on motility and secretion is contraindicated.

## SUMMARY AND CONCLUSIONS

1. Twelve patients with peptic ulcer were given enterogastrone orally in doses of 8 to 16 Gm. daily for periods up to eleven months. Recurrence of typical symptoms of ulcer occurred in 2 of these patients while they were under treatment.

2. Sixteen patients with peptic ulcer were given intramuscular injections of 200 mg. of enterogastrone daily for periods up to nine months. Three of the patients had either recurrence or persistence of symptoms while they were under treatment.

3. For 17 of the 28 patients treated roentgenograms of the upper gastrointestinal tract were available from the start of therapy. The

roentgenologic appearance of the lesion after therapy was improved in 6 cases, unchanged in 8 cases and definitely worse in 3 cases.

4. Single intramuscular injections of 200 to 800 mg. of enterogastrone in persons with peptic ulcer produced no changes in the volume of fasting gastric secretion, output of hydrochloric acid, pepsin concentration or gastric motility.

5. Daily administration of enterogastrone orally or parenterally for periods up to eleven months to persons with peptic ulcer caused no significant alterations in the volume of fasting gastric secretion, volume of hydrochloric acid, pepsin concentration or type of response to a caffeine test meal. This was true whether there was evidence that the peptic ulcer improved, remained stationary or became worse.

# PERITONEAL REACTION TO OXIDIZED CELLULOSE

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ST. LOUIS

RECENTLY there has been added to the armamentarium of the surgeon a gauzelike material which is completely absorbed in the tissues and serous cavities. This material is known as oxidized cellulose. Its physical and chemical properties have already been thoroughly described in the literature.

There has always been some concern expressed about leaving nonabsorbable materials in tissues and especially in the serous cavities. Nonabsorbable sutures such as silk, cotton or nylon may be left in the tissues and serous cavities with a certain degree of impunity. Gauze sponges and packs have been left in the serous cavities with untoward results such as empyema, fistula formation and intestinal obstruction. They have also been left in the serous cavities for hemostasis, and when they have been removed hemorrhage has often recurred or infection has been introduced.

The use of oxidized cellulose with thrombin as a hemostatic agent has been studied by Uihlein and his co-workers.[2] A specific hemostatic action of its own which is due to the formation of a coagulum consisting of the salts of cellulosic acid and hemoglobin was observed by Frantz and Lattes.[3] These same authors also observed that oxidized cellulose had an untoward effect in bone.[4] There was a delay in early callus formation in fractures which was due to the acidity of the gauze. Ultimately, however, healing did occur. The following statement was noted

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From the Department of Surgery, St. Louis University School of Medicine.

The material with which this work was done was supplied free of charge by Parke, Davis and Company, Detroit.

1. Seegers, W. H., and Doub, L.: Oxidized Cellulose and Thrombin, Proc. Soc. Exper. Biol. & Med. **56**:72, 1944. Unruh, C. O., and Kenyon, W. O.: Investigation of the Properties of Cellulose Oxidized by Nitrogen Dioxide, J. Am. Chem. Soc. **64**:127, 1942. Yackel, E. C., and Kenyon, W. O.: The Oxidation of Cellulose by Nitrogen Dioxide, ibid. **64**:121, 1942.

2. Uihlein, A.; Clagett, O. T.; Osterberg, A. E., and Bennett, W. A.: Absorbable Oxidized Cellulose with Thrombin as a Hemostatic Agent in Surgical Procedures, Surg., Gynec. & Obst. **80**:470, 1945.

3. Frantz, V. K., and Lattes, R.: Oxidized Cellulose—Absorbable Gauze (Cellulosic Acid), J. A. M. A. **129**:798 (Nov. 17) 1945.

4. Lattes, R., and Frantz, V. K.: Absorbable Gauze in Bone Surgery, Ann. Surg. **124**:28, 1946.

in an article by Frantz and her co-workers [5] on the use of oxidized cellulose in serous cavities: "The work on serous cavities is not complete as regards the study of adhesions, but is reported here to illustrate the tissue reaction to large amounts of gauze." Burns [6] recently studied the tissue reaction to oxidized cellulose and the fate of the latter in the peritoneal cavity and found no foreign body, no formation of permanent adhesions and complete absorption of the gauze.

Heretofore, healthy and intact serosal surfaces were observed, but it is the traumatized serosal surface in which the surgeon is primarily interested. It is the purpose of this study to carry further the investigation suggested by Frantz and her co-workers and begun by Burns.

Experiments were carried out in which ordinary mongrel dogs of various size and weight and of both sexes were used. Anesthesia was obtained by using pentobarbital sodium intravenously. The surgical procedures were carried out with the sterile technic, a right rectus incision for the initial laparotomy and a left rectus incision for subsequent observation being used. The animals were healthy, and the peritoneal cavities were free from infection. Two groups of animals were used, one group consisting of 20 animals and another, used as a control, consisting of 5.

In the first series of animals a loop of ileum was brought out and an area approximately 4 by 1.5 cm. was denuded of its serosa by being scraped with a scalpel. The intestine was protected from drying with moist sponges, since drying of the serosa in itself predisposes to the formation of adhesions. The oozing produced by scraping was controlled with warm moist sponges. A piece of oxidized cellulose of 5 by 2 cm. and of 8 ply thickness was applied to the denuded area and held in place by four interrupted silk sutures. These sutures were placed at the corners of the oxidized cellulose and did not come in contact with the denuded area so that any tissue reaction to the silk would not affect the area to be studied.

A total of 20 animals were used in this series and divided into four groups of 5 animals each. The four groups of animals were reoperated on one, two, three and four weeks respectively after the initial operation. It has been demonstrated by previous work that complete absorption of oxidized cellulose occurs within four weeks. Therefore four weeks was the maximum time interval used.

Grossly, there was no significant difference between the appearance of the intestines at the end of one week and that at the end of four weeks. There was a small light brown spot, previously recognized as

5. Frantz, V. K.; Clarke, H. T., and Lattes, R.: Hemostasis with Absorbable Gauze, Ann. Surg. **120**:181, 1944.

6. Burns, F. J.: Reaction of Tissue to and the Fate of Oxidized Cellulose in the Peritoneal Cavity of the Dog, Arch. Surg. **53**:348 (Sept.) 1946.

oxidized cellulose, at the site where the oxidized cellulose had been placed in 50 per cent of the animals. The omentum was adherent to the intestine at the site of the trauma, and there were fine adhesions present between the adjacent loops of intestine. Of the animals reoperated on

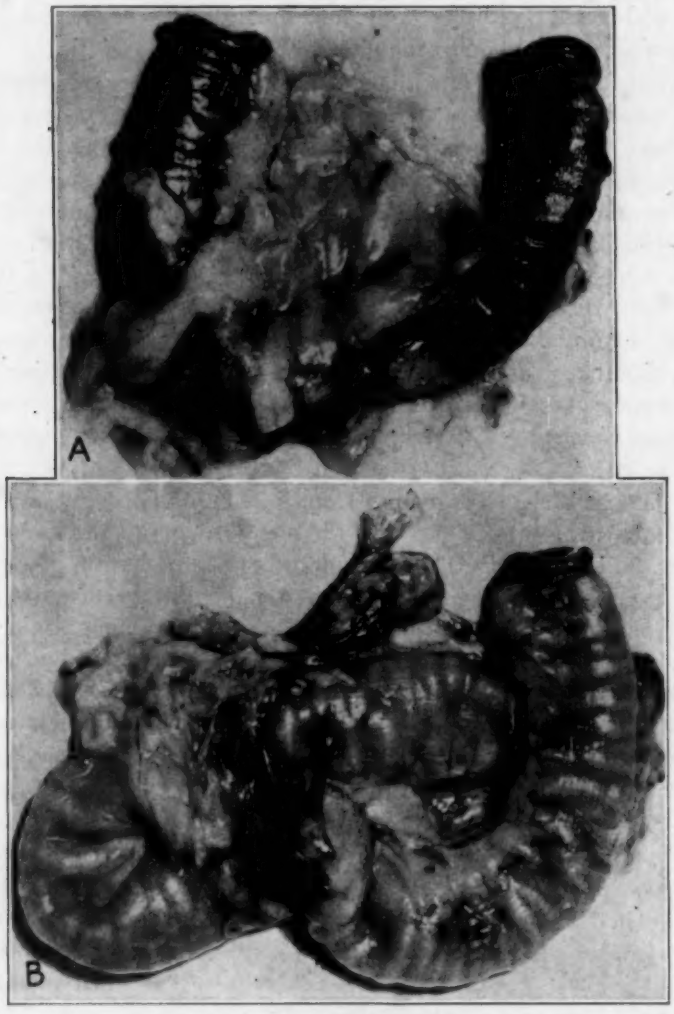


Fig. 1.—Omental adhesions after the immediate application of oxidized cellulose. *A*, one week after; *B*, two weeks after.

after two and three weeks, there were 2 animals in each group in which the intestine and the omentum were adherent to the anterior abdominal wall at the site of the previous incision. This was not noticed in any of the animals reoperated on after one and four weeks (figs. 1 and 2).

Microscopically, the following tissue reaction was noted after one week: The adjacent segments of intestine were held together by a cellular layer which was composed chiefly of young fibroblasts, newly

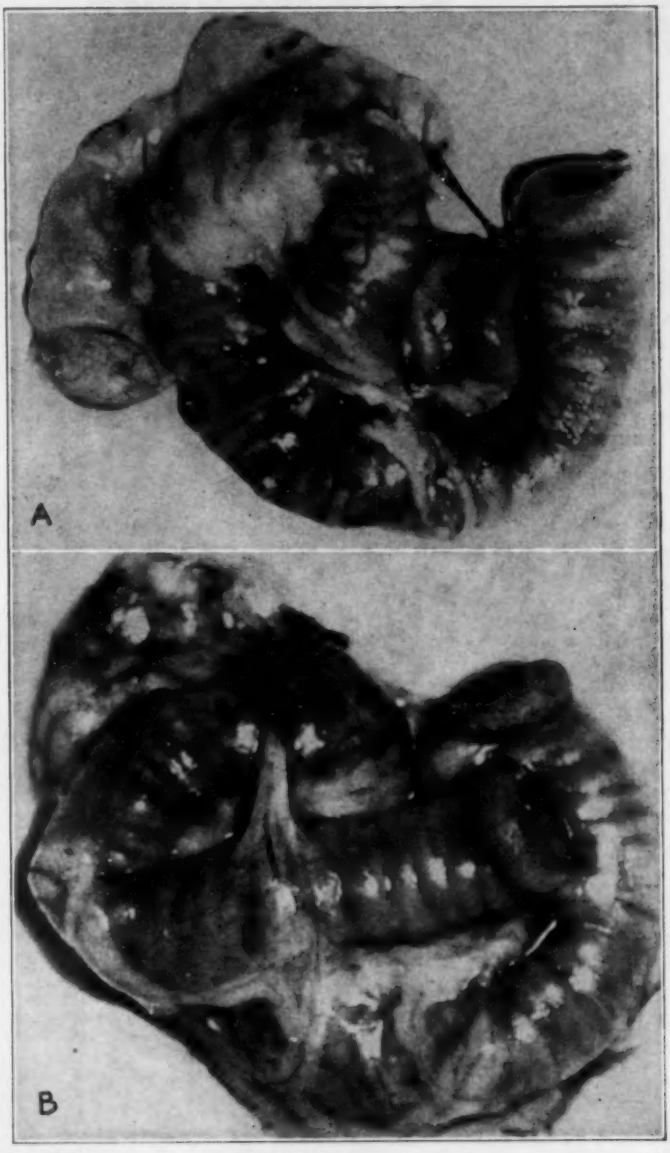


Fig. 2.—Omental adhesions after the immediate application of oxidized cellulose. *A*, three weeks after; *B*, four weeks after.

formed capillaries, small round cells and macrophages. There were several tubercle-like areas which were made up of a Langhans type of

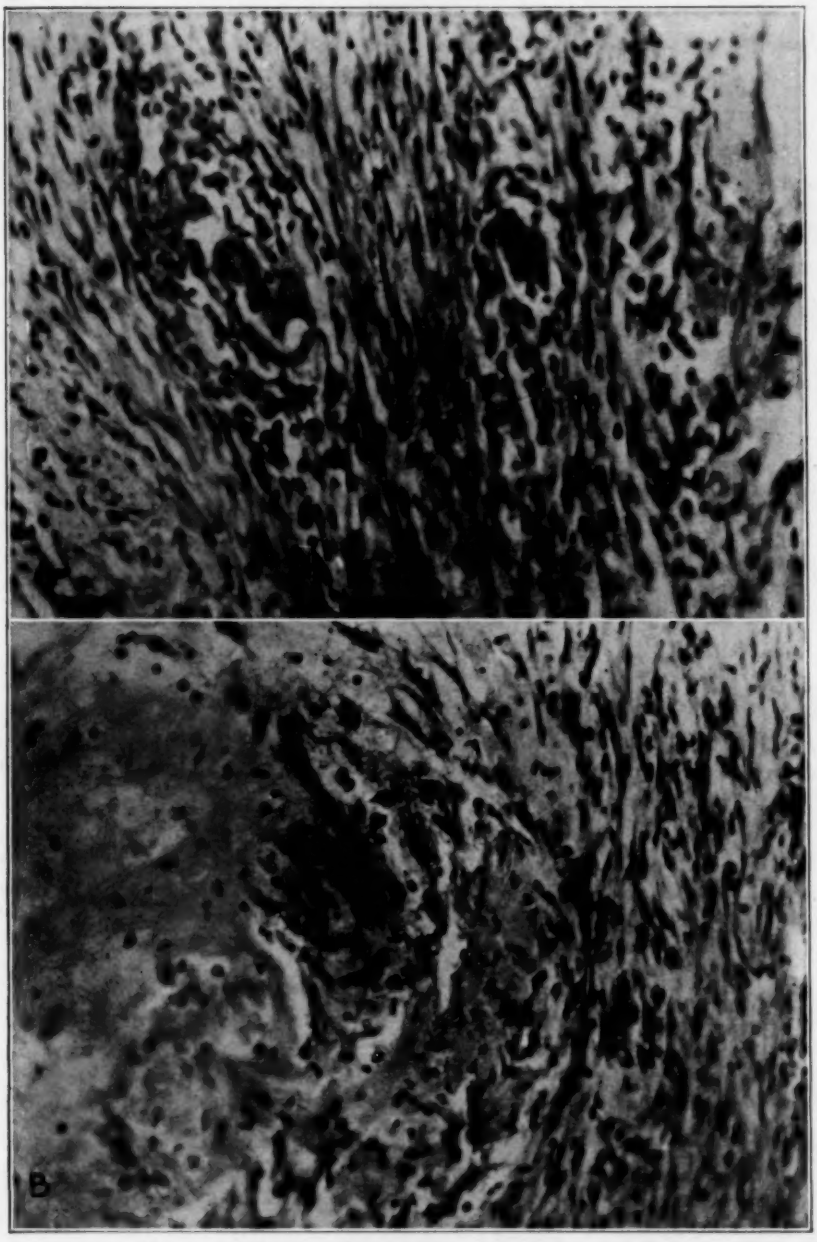


Fig. 3.—*A*, the tubercle-like areas and cellular stroma noted. *B*, the organization of the exudate.

giant cell surrounded by a collar of young fibroblasts. In several areas the giant cells were engulfing small particles of oxidized cellulose. A cystic area was found in 1 animal only. It contained edema fluid, macrophages, some ghost erythrocytes and occasional polymorphonuclear neutrophils. At one end of this cystic area there was evidence of organization of the exudate (fig. 3).

After two weeks the cellular layer between the adjacent segments of intestine was found to be thicker than it had been at the end of one week. The fibroblasts were mature and surrounded by collagenous connective tissue. The tubercle-like reaction was found to be more pro-

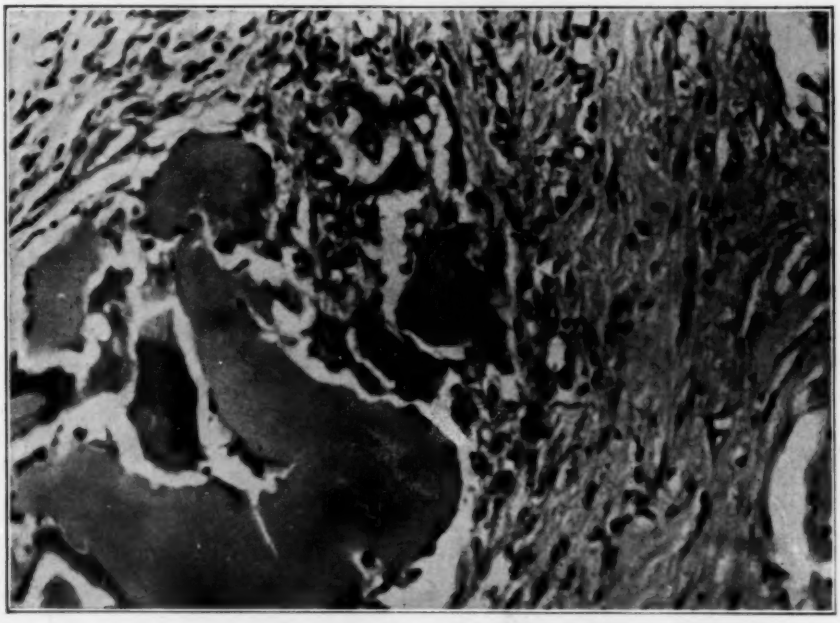

Fig. 4.—Pronounced tubercle-like reaction about the oxidized cellulose.

nounced. The cellular stroma consisted of macrophages containing a deep basophilic-staining material. These were considered to be characteristic and almost diagnostic of oxidized cellulose (fig. 4).

Three weeks after the application of the oxidized cellulose the thickness of the cellular layer covering the intestine was less than it had been after the first and second weeks. The stroma was loosely fibroblastic, with some small round cell infiltration. The surface was smooth and lined by a single layer of elongated cells similar to those of normal peritoneum. Beneath this, or subserosally, was the loose fibroblastic stroma with small round cells, and in the deeper portion of this layer there were characteristic macrophages and remnants of the oxi-

**Fig. 5.**—*A*, loose fibroblastic stroma and relatively smooth surface. *B*, macrophages and remnants of oxidized cellulose.

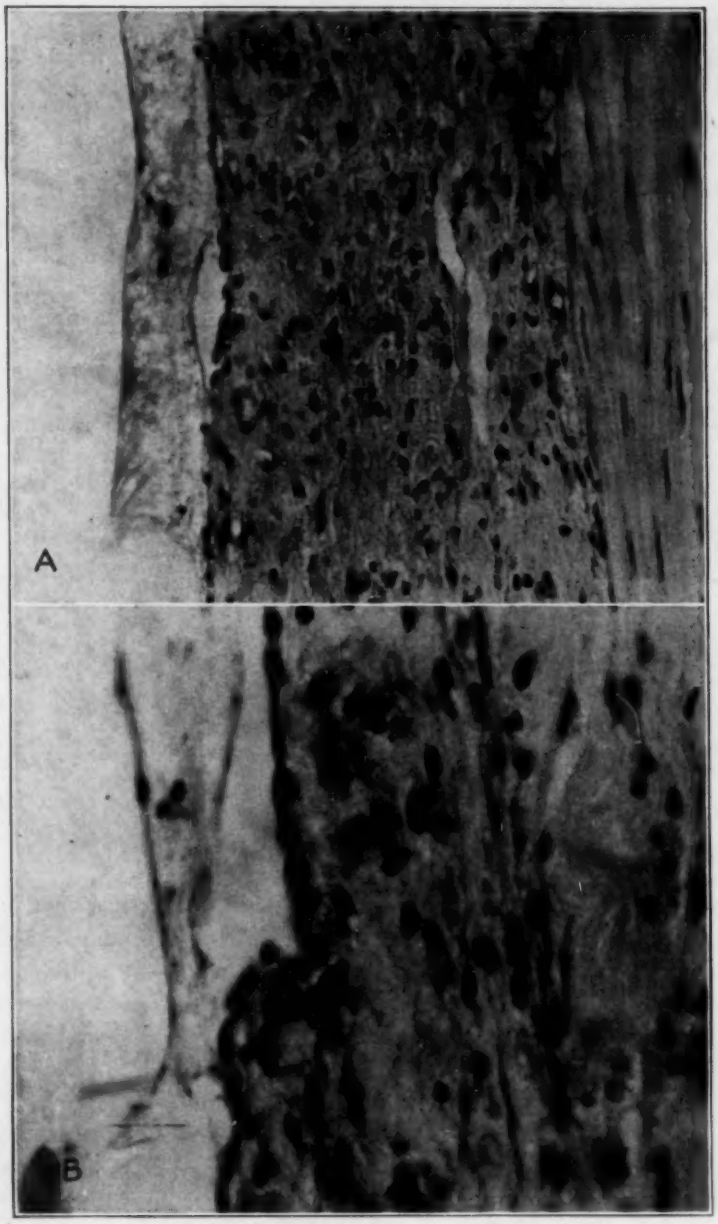


Fig. 6—*A*, decreased thickness of the cellular layer and single layer of lining cells. *B*, high power magnification of the tissue in *A*, demonstrating the single layer of lining cells.

dized cellulose in the stroma. The tubercle-like reaction and the giant cells previously observed were absent at this time (fig. 5).

At the end of four weeks the layer covering the intestine was thinner than previously and the surface was composed of a single layer of flattened and elongated cells resembling those of normal peritoneum. The subserosal layer was composed of loosely arranged fibroblasts, with occasional small round cells scattered throughout. In the deeper portion of the subserosa characteristic macrophages were present. Again there were no giant cells, and no tubercle-like reaction was noted. This closely resembled normal peritoneum except for the increased thickness (fig. 6).

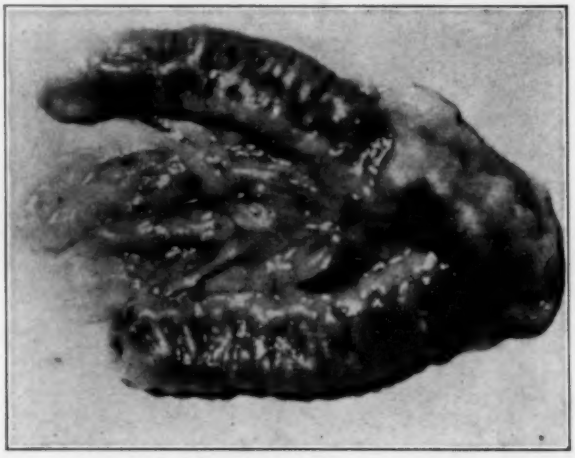

Fig. 7.—Demonstration of the more pronounced omental adhesions.

In a second series of 5 animals a loop of ileum was traumatized as described previously and the oozing controlled with warm moist sponges. The ileum was returned to the peritoneal cavity and the abdominal incision closed. At the end of one week the animals were reoperated on. The rather numerous firm adhesions present between the omentum and the traumatized ileum were separated. A piece of 8 ply oxidized cellulose large enough to cover the raw surface produced by separating the adhesions was sutured to the ileum. The animals were then reoperated on after eighteen to twenty days so that any possible effect that oxidized cellulose might have on the recurrence of adhesions would be observed.

The gross physical findings were the same in all 5 animals. The omentum was adherent to the ileum at the site of the oxidized cellulose, and there were many adhesions present between this segment of ileum

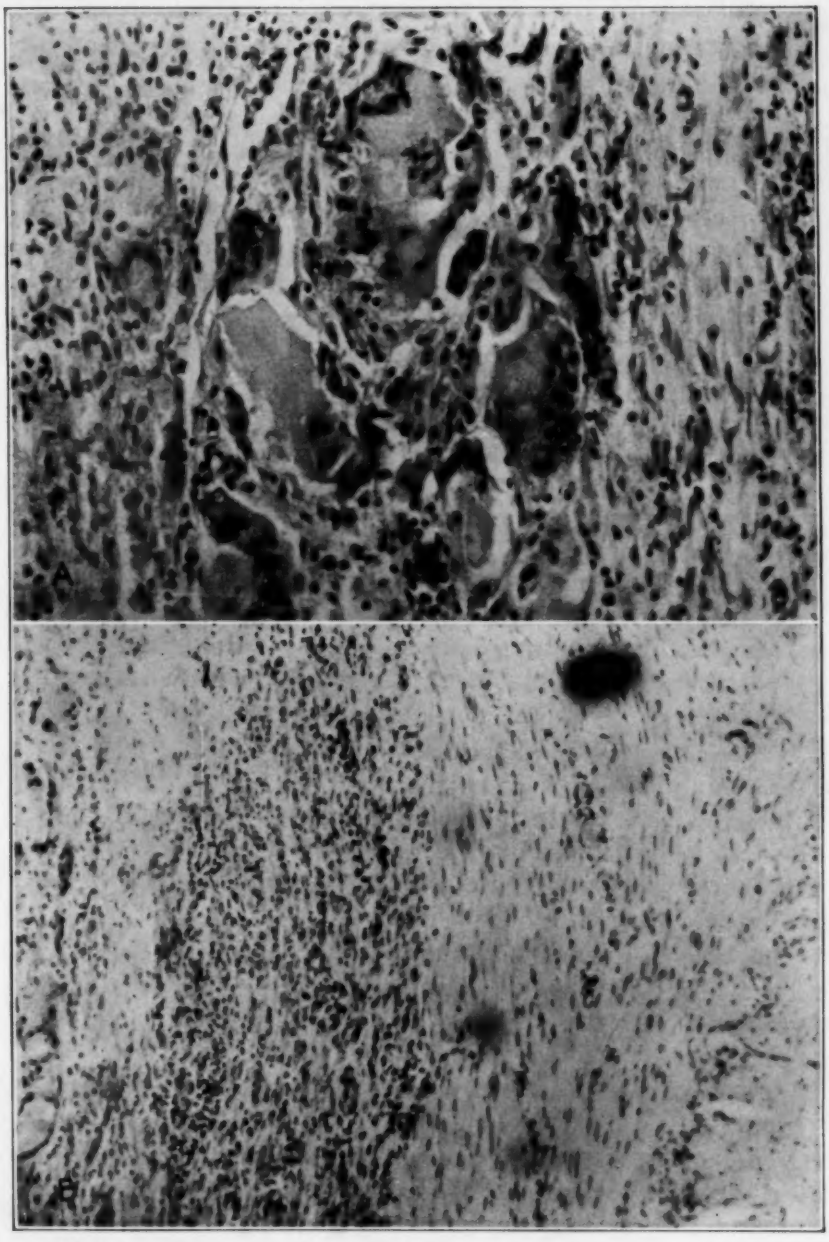


Fig. 8—*A*, increased tubercle-like reaction. *B*, pronounced cellular stroma of fibroblasts, capillaries and round cells.

and the adjacent loops of intestine. This was more pronounced than in the first series of animals. It would seem from these results that oxidized cellulose does not prevent the recurrence of adhesions (fig. 7).

Microscopically the tissue reaction was similar to that described previously for the animals used in the first series of this experimental study. The cellular stroma composed of young fibroblasts, newly formed capillaries, an infiltration of small round cells and characteristic macrophages was covering the surface of the intestine. Syncitial-like cells were seen engulfing remnants of oxidized cellulose. The tubercle-like reaction was more predominant than in those animals in which the oxidized cellulose was applied immediately (fig. 8).

## COMMENT

Little has been added to the literature as a result of this experimental study. The brown spot observed, which has been identified previously as oxidized cellulose, was present on the surface of the intestine in 50 per cent of the animals. The immediate application of oxidized cellulose to traumatized serosa is better for the prevention of adhesions than reoperation and the use of oxidized cellulose. The adhesions observed in the animals in which the oxidized cellulose was applied immediately were finer and fewer than in those animals in which it was applied one week after the trauma. In the latter the adhesions were more numerous and firmer.

The reaction of traumatized peritoneum to oxidized cellulose is a fibroblastic proliferation arising from the exposed connective tissue. This connective tissue changes form and becomes flattened, resulting in a lining membrane similar to normal peritoneum. This is in accordance with the work of Clarke [7] on experimental mesothelium and with that of Hertzler [8] on peritoneal healing.

The tubercle-like reaction, with suggestive giant cell formation, is evidently due to the arrangement of the deeply basophilic-staining macrophages around the particles of oxidized cellulose, which produces a picture simulating syncitial-like cells.

In previous work on the intact peritoneum permanent adhesions were not observed. Adhesions are definitely produced and are permanent. They are undoubtedly an important part of the process of healing, as stated by Hertzler.[8] Once adhesions have been formed, their recurrence cannot be prevented by applying oxidized cellulose to the site of previous trauma to the peritoneum.

7. Clarke, W. C.: Experimental Mesothelium, Anat. Rec. **10**:301, 1916.
8. Hertzler, A. E.: The Peritoneum, St. Louis, C. V. Mosby Company, 1919.

SUMMARY

1. The primary reaction of traumatized peritoneum to oxidized cellulose is a fibroblastic proliferation.

2. The connective tissue becomes flattened to produce a lining membrane.

3. Adhesions are formed between the omentum and intestine and the adjacent segments of intestine.

4. The adhesions are permanent and are present after complete absorption of the oxidized cellulose.

5. The adhesions observed after immediate application of oxidized cellulose to the traumatized serosa are finer and less numerous.

6. The recurrence of adhesions cannot be prevented by oxidized cellulose.

University Club Building.

# APPLICATION OF DELAYED SUTURE IN THE MANAGEMENT OF WOUNDS

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THE DEVELOPMENT of a large scale, coordinated program of "reparative surgery" was a brilliant achievement of the recent war.[1] With conservation and rehabilitation of fighting man power as the ultimate goal, delayed suture, or secondary closure of wounds, evolved into one of the most important contributions in this expanded program of "reparative surgery."

In the development of our present concept of delayed suture, several formalities, technics or methods of closure were utilized, each having its ardent advocates. One of these, that of preliminary inspection, bacteriologic studies and the application of wet dressings before an attempt at closure, was found to be not only unnecessary but actually unfavorable to best results. Unless there was obvious evidence of sepsis, a fixed policy was adopted of leaving the initial dressing undisturbed until the patient arrived in the operating room. At that time the wounds were evaluated, and unless infection was grossly apparent they were immediately closed by whatever means seemed applicable, including skin graft. The methods of closure utilized included: (1) simple closure (no trimming, excision or undermining); (2) trimming and undermining of the edges of skin, followed by suture and (3) complete excision of the wound, followed by suture.

In an effort to determine which method produced the best results, a careful analysis of 360 consecutive, unselected cases, including 721 wounds, was recorded. These wounds included those complicated by compound fractures, nerve injuries, amputations and abdominal and thoracic injuries.

This study revealed that it was not the severity of the wound, its location or the method of closure which determined the success, failure or degree of healing. It has been graphically demonstrated that the time

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From the Department of Research Surgery of the Ohio State University.

Read at the fourth annual meeting of the Central Surgical Association, Chicago, Feb. 22, 1947.

1. Churchill, E. D.: The Surgical Management of the Wounded in the Mediterranean Theatre at the Time of the Fall of Rome, Ann. Surg. **120**:268, 1944.

interval between the initial operation and delayed suture is the all-important factor (chart). Furthermore, this time interval frequently determined the technic to be utilized in delayed suture.

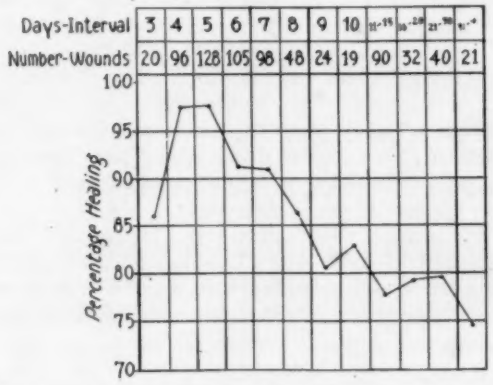
The following salient points were learned from this analysis:

1. There were 512 wounds in which 100 per cent healing occurred; in three fourths of these there was a time interval of seven days or less between the initial operation and delayed suture.

2. The optimum time interval between initial operation and delayed suture was four to five days.

3. Ninety-seven per cent of the healing occurred in this time interval, as compared to 78 per cent healing when the time interval was in excess of ten days.

4. The over-all degree of healing for the 721 wounds was 88.4 per cent.




Time interval in days from the primary to the secondary operation.

5. Seventy-two per cent of the patients whose wounds were closed in six days or less returned to duty in an average of twenty-seven days, whereas only 49 per cent returned to duty in an average of thirty-two days when the time interval was seven days or more.

6. Infections of varying degree were encountered in 111 (15 per cent) of the wounds preoperatively and in 154 (21 per cent) of the wounds postoperatively. However, in only 29 of the wounds discovered to be infected postoperatively was the infection severe enough to result in a total failure of the closure or skin graft. Of these, 19 had been infected preoperatively.

Delayed suture of wounds is now an established procedure which can with advantage be adapted to the management of traumatic wounds in civilians associated with severe contamination, marked destruction of

tissue or prolonged lag between injury and treatment. It is earnestly to be hoped that the method will not again be relegated to archival oblivion, as occurred after the last war.

## DISCUSSION

DR. JACOB BERMAN, Indianapolis: I should like to discuss Dr. Lowry's paper. This work is a useful contribution since surgery is essentially a study of wounds and wound healing. Certainly his observations should be taken seriously. It is almost unbelievable that he should come to the identical conclusions that my colleagues and I came to in 1943, working in the experimental laboratory. This paper was published in *Surgery, Gynecology and Obstetrics* in August 1943. The work was done on guinea pigs. We made an abdominal incision and introduced a virulent culture of Staphylococcus aureus which we had obtained from a patient with a carbuncle. Incisions were made in the abdominal wall and cultures introduced into the wounds at the end of twelve, twenty-four, forty-eight, seventy-two, ninety-six, one hundred and twenty and one hundred and forty-four hours. We reversed the procedure, making incisions on each day. On the sixth day all wounds were inoculated. The results were the same in the two groups.

We found that on about the fifth day we could rub this culture of staphylococci in a wound with no more reaction than occurred with sterile water. We discovered that if we made another incision in the lower portion of the abdomen and introduced the virulent culture in the second wound infection occurred every time.

We concluded that wound immunity was at low ebb within the first eighteen to twenty-four hours. Then immunity began to pick up and reached a maximum on about the fifth or sixth day. We decided that it was a local immunity because the wound in the upper part of the abdomen did not protect any other part of the abdominal wall outside of the zone of granulation tissue.

During the war, I was given a reprint of a paper by Sargeant and Morton which appeared in the *Lancet* of Sept. 9, 1944. They had followed our suggestions in the treatment of one hundred and forty-three soft tissue wounds in soldiers in the Mediterranean Theater and concluded that the best time for suture was between the fifth and the ninth day after injury.

Our conclusions were that if a wound is seen within the first eight hours the classic method of débridement should be used and if it is seen within twenty-four to forty-eight hours débridement may be done and tendons and nerves approximated but the wound should not be closed. After forty-eight hours, it is not wise to molest the wound in any way. It is best to protect it with sterile dressings and to allow the patient to rest until the fifth day. Then the injury may be cleaned and the wounds sutured.

In applying our work clinically, we have classified wounds as early, early late and late late. We define early wounds as those seen within six to eight hours if the wound is made by a blunt instrument; if it is made by a sharp instrument, the period may be greatly extended. We consider the early late wounds as those seen within the first twenty-four to forty-eight hours. We clean these wounds, and bring the tendons and nerves together, leaving a gap of one fourth of an inch in the skin suture line. Late late wounds are those seen after forty-eight hours or those which have had iodine or other strong antiseptics poured into them. With these wounds it is probably better to wait until the fifth to the seventh day, when local immunity has been established, before anything is done.

# REVIEW OF UROLOGIC SURGERY

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## KIDNEY

*Anomaly.*—Hepler [1] reports a case of a girl, 5 years old, who had bilateral duplication of the renal pelves and ureters, with hydronephrotic destruction of both halves of the right kidney and the upper half of the left. The ureter from the latter opened into the uterine cervix.

The embryonic features of this rare anomaly are discussed, particularly in relation to the disputed true vaginal and uterine ectopic ureteral openings.

The diagnostic problems and the difficulty of roentgenographic demonstration of the anomalous renal segments and ureters, when the former are practically functionless, are demonstrated.

After right nephroureterectomy was done, the incontinence was cured by complete removal of the ureter to the anomalous segment of the left kidney.

Bacon [2] states that a supernumerary kidney is the rarest congenital renal anomaly. The abnormality must be clearly differentiated from double or fused kidneys, in that the accessory third organ is a "distinct, encapsulated, large or small parenchymatous mass topographically related

1. Hepler, A. B.: Bilateral Pelvic and Ureteral Duplication with Uterine Ectopic Ureter, J. Urol. **57**:94-105 (Jan.) 1947.

2. Bacon, S. K.: Large Hydronephrosis of a True Supernumerary Kidney, J. Urol. **57**:459-466 (March) 1947.

to the usual kidney by a loose, cellular attachment at most and often by no attachment whatsoever."

Development deviations of the urinary tract early in embryonic life are responsible for the origin of a true supernumerary kidney. This anomaly occurs when completely duplicated or bifurcated excretory ducts extend cranially to enter two independent metanephrogenic masses. They continue to develop into two separate renal entities without fusion, each with its capsule and ureter. The ureter may have an independent ending intravesically or extravesically, or it may join the other ureter on the same side.

Renal and ureteral anomalies predispose to pathologic lesions. The majority of reported cases of supernumerary kidney reveal clinical manifestations of disease during life, either primary in the accessory kidney or as an associated observation.

Bacon's patient was a woman aged 47 years. Physical examination revealed a large cystic mass occupying the entire right side of the abdomen and extending across the median line. Cystoscopic investigation revealed two normal-appearing ureteral meatuses, with complete urinary inactivity of the right. The ureters were catheterized to the renal pelves, without evidence of obstruction. The catheter in the right ureter seemed to enter a large cavity and could have been introduced many more centimeters. It rapidly drained dilute clear urine, which contained an occasional pus cell, erythrocytes and no bacteria. Urine obtained from the left kidney was normal. Indigo carmine injected intravenously appeared in five minutes from the left kidney, in excellent concentration; none appeared from the right. A precystoscopic roentgenogram of the kidneys, ureters and bladder disclosed a large homogeneous area of density on the right side. A plain roentgenogram taken after ureteral catheterization revealed the abnormal mass, the right ureteral catheter displaced to the medium line and the upper half of a normal-appearing right kidney high up in the costovertebral area.

A bilateral pyelogram, taken after injection of 200 cc. of methiodal sodium ("skiodan"), a radiopaque medium, into the right kidney and 7 cc. into the left, revealed extensive hydronephrosis on the right, with normal-appearing renal substance above it. A catheter was anchored in place in the hydronephrotic sac to provide continuous drainage, and the abdominal mass disappeared. Two days later the catheter was expelled spontaneously and was replaced by a larger one. A right pyelogram made at this time emphasized more definitely the presence of additional renal tissue located above the hydronephrotic sac, as well as the unusually low situation of the latter, its center being opposite the lumbosacral articulation. At operation it was concluded that a normally formed right kidney existed above the hydronephrosis.

The retroperitoneal region was exposed on the right through a curved incision in the costoiliac space, and two separate kidneys were promptly observed. There was no evidence of loose cellular attachments. The higher organ was normal in appearance and consistency, and its ureter proceeded downward and disappeared behind the large accessory organ. The caudal supernumerary kidney was the site of extensive hydronephrosis. The sac was densely adherent to the peritoneum, ascending colon and inferior vena cava. This sac was cautiously removed in sections by blunt and sharp dissection. Its ureter was ligated at the ureteropelvic juncture, and the atrophic renal pedicle, although poorly defined, was uneventfully accommodated in one ligature.

Postoperative progress in the hospital was not remarkable. On the eleventh day cystoscopic investigation of the remaining urinary tract on the right was carried out. Indigo carmine injected intravenously appeared at the right and left ureteral meatuses in seven and four and a half minutes, respectively. Excretion from the right ureter was moderately well concentrated, and from the left it was excellently concentrated. On catheterization of the right ureter, obstruction was encountered 14 cm. from the bladder; however, serial pyeloureterograms, made after insertion of a large catheter, were successful. These roentgenograms revealed moderate hydronephrosis of the upper part of the remaining kidney, ureteral tortuosity and stricture in the lumbar region and extravasation of opaque medium in the iliac area through the ureteral stump, near the site of bifurcation.

Although there were no postoperative symptoms indicative of renal and ureteral disease of the right side, a program of dilatation of the right ureter and serial pyeloureterograms was instituted. Roentgenograms still revealed considerable reduction in size of the renal pelvis and more normal-appearing minor calices. Although ureteral stricture was remarkably pronounced roentgenographically, it was scarcely noticeable with the dilating instrument and produced no clinical signs.

*Neoplasm.*—Harvey [3] observed that 81.5 per cent of a series of fifty-four tumors of the renal pelvis and cortex occurred in the fifth, sixth and seventh decades of life and that 70 per cent were in men. Hematuria was the commonest initial or early symptom in the cases of operable tumor, whereas metastatic symptoms were the most frequent early features in the cases in which the tumor was inoperable or in which there was necropsy. Microscopic studies of the urine in 44 cases revealed red cells in 77 per cent, whereas the incidence of gross hematuria in the whole series was 59 per cent. Proteinuria, which was

3. Harvey, N. A.: Kidney Tumors: A Clinical and Pathological Study, with Special Reference to the "Hypernephroid" Tumors, J. Urol. **57**:669-692 (April) 1947.

the most frequent urinary observation, occurred in 93 per cent of cases. The value of the intravenous pyelogram in obscure cases and as a preliminary procedure is stressed. The common sites of metastatic lesions and the mechanism involved are discussed. The discriminating use of irradiation is called for in some cases. The survival period depends on several variables, including size of the tumor, age and grade of malignancy. The nature of the hypernephroid tumor is discussed, and the literature is briefly reviewed with special reference to the Grawitz theory and the relations between the renal adenoma and adenocarcinoma. In Harvey's opinion the Grawitz theory is untenable as an explanation of the histogenesis of the large majority of malignant lesions of the renal cortex.

Senger, Bottone and Murray [4] report a case of bilateral hypernephroid carcinoma in which pyelograms showed the progressive development of the tumor in the solitary kidney. Results of biopsy of the tumor in the solitary kidney are reported.

This is the first case of bilateral hypernephroma in a female patient reported in the literature and the second case in which biopsy has been obtained to prove tumor in the remaining kidney.

The literature has been reviewed and summarized to bring the total number of reported cases of bilateral hypernephroma to 17.

Dodson [5] discusses the surgical treatment of polycystic disease of the kidney and reports observations in 2 cases. In polycystic disease the destruction of renal tissue results from pressure exerted by the gradual increase in the size of congenital cysts interspersed throughout the kidney. Most patients who have polycystic kidneys are more than 30 years of age before the disease is recognized. Therefore, it is evident that the cysts grow slowly and many years are usually required for the disease to manifest itself clinically. It seems logical to operate on these patients as soon as the disease is recognized, to excise a portion of the wall of each superficial cyst and aspirate as many as possible of the more deeply situated cysts. Recent experience with 2 cases of polycystic kidneys, in which surgical treatment was employed, causes him to question his former conservative attitude toward this disease.

Medical treatment has little to offer these patients except general supervision and advice as to mode of living and diet. The progress in all cases is constantly, even though many times gradually, downhill. More consideration should be given to the probability of surgical relief for many of these patients.

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4. Senger, F. L.; Bottone, J. J., and Murray, G. E.: Bilateral Hypernephroma: Case Report, J. Urol. **57**:106-115 (Jan.) 1947.

5. Dodson, A. I.: The Surgical Treatment of Polycystic Disease of the Kidney: Case Reports, J. Urol. **57**:209-212 (Feb.) 1947.

*Stone.*—Engel [6] reports a series of 9 cases in which partial nephrectomy had been done for caliectasis with stone and in which the patients had been followed for five or more years. Engel states that the operation is indicated in all cases in which stones are present in dilated calices and there is evidence of infundibular constriction and that this is especially applicable when the upper or lower calices are involved and the remainder of the renal pelvis is essentially normal. The removal of the pathologic calix reduces the likelihood of recurrent stone, and no recurrence has been observed in any case in this series in from five to twelve years following operation. In all cases, infection in the kidney cleared up after operation. The operation carries with it no greater risk or morbidity than other operations for renal stone. There were no deaths in this series of cases. In all cases, satisfactory renal function has been demonstrated in the remaining portion of the resected kidney, and this function was sufficient to maintain life if disease or injury should destroy the opposite kidney.

Abeshouse,[7] in discussing Engel's paper, recalls an earlier paper in which he reviewed 77 cases collected from the literature in which caliectasis was treated by partial nephrectomy, adding 3 cases from his own practice. The localized process was described as calculous pyonephrosis in 58 cases, pyonephrosis in 11 cases and hydronephrosis in 11 cases. Three deaths followed operation, a mortality rate of 3.8 per cent, which compares favorably with a mortality rate of 7 to 21.3 per cent for nephrectomy for similar conditions. Secondary hemorrhage did not occur in a single case. Postoperative urinary fistula was reported in 2 cases. Secondary nephrectomy was required in 3 cases.

Abeshouse states that partial nephrectomy is particularly efficacious when the disease process is confined to the upper or lower major calix but that it may not be feasible or practical when the middle major calix is involved. Resection of the diseased region involving a terminal calix decreases the incidence of complications, that is, hemorrhage, urinary fistula and formation of stone, which develop as a result of faulty hemostasis, inadequate drainage and urinary stasis following the customary treatment of the sacculated region by incision and drainage with gauze packs.

Partial nephrectomy is the operation of choice when the following criteria can be fulfilled:

1. The disease process must be sharply confined to one part of the kidney as determined at operation.

2. The operation for removal of the affected portion of the kidney can be performed with ease and without undue risk to the patient.

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6. Engel, W. J.: The Late Results of Partial Nephrectomy for Calyectasis with Stone, J. Urol. **57**:619-630 (April) 1947.

7. Abeshouse, B. S., in discussion on Engel,[6] pp. 631-633.

3. The blood supply to the portion of the kidney remaining after resection must be adequate.

4. The portion of the kidney remaining after resection should be able to carry at least a half or more of the secretory burden of the affected kidney.

5. The ureter of the resected kidney must be healthy and intact.

The two main complications following this operation are: (1) primary or secondary hemorrhage and (2) urinary fistula. These complications occurred more frequently in the early period of renal surgery, as a result of either faulty hemostasis with gauze packs or improper closure of the renal wound. Urinary fistula may be the result of incomplete removal of the pathologic tissue, faulty closure of the opened calix, persistence of obstruction in ureter or calix and persistence of the opening resulting from nephrostomy or pyelostomy. When the operation is performed in a careful manner, the end results are so uniformly satisfactory that the surgeon is more than amply rewarded for his painstaking effort. However, certain anatomic, pathologic and technical difficulties may contraindicate partial nephrectomy.

Suby and Suby [8] state that certain types of bacteria, after entering the urinary tract, possess the power to split urea, form ammonia and alkalize the urine. This has been a common clinical observation. A similar pathologic sequence has been produced experimentally in rabbits, with artificial hydronephrosis, by giving them intravenous injections of organisms recovered from the urine of patients who have calcium phosphate renal stones. It has been noted that in rabbits with anatomically normal kidneys alkalization of the urine, following infection, is usually a transient phenomenon, without resulting formation of calculi. In rabbits with artificial hydronephrosis, however, infection with urea-splitting organisms has produced renal stones. Infections of the urinary tract in human beings often follow or are concomitant with infections elsewhere in the body. The fact that apparently the same organism was recovered from both the socket of a tooth and the urine of a patient whose urinary difficulties started with abscessed teeth suggests that transient bacteremia had existed. This method of producing renal stones in animals furnishes excellent subjects for experimentation for further study of the dissolution of calcium phosphate urinary stones.

*Inflammatory Conditions.*—Mathé [9] presents a review of 98 cases of renal tuberculosis. Eighty-one of these were cases of unilateral renal

8. Suby, H. I., and Suby, R. M.: Experimental Production of Kidney Stones with Urea-Splitting Organisms, J. Urol. **57**:995-1000 (June) 1947.

9. Mathé, C. P.: Unilateral Renal Tuberculosis: Management of the Nephrectomized Patient; Review of Ninety-Eight Cases, J. Urol. **57**:451-458 (March) 1947.

tuberculosis in which treatment was by nephrectomy. Certain advances in operative technic have been emphasized, which aid in reducing mortality and healing of the wound after nephrectomy. The importance of the one stage ureteronephrectomy when tuberculosis of the ureter coexists with tuberculosis of the kidney has been stressed, and the value of a two stage nephrectomy for the critically ill patient when tuberculosis of the kidney is complicated by shock, extreme debility, perinephric abscess and so forth has been emphasized. Lavage of the wound with penicillin in isotonic solution of sodium chloride to control secondary infection assures prompt healing, and there is less likelihood of postoperative abscess or formation of sinuses. In 4 cases, in which postoperative examination and treatment were omitted, diversion of the urinary stream was later necessary, because of sepsis and uremia.

Analysis of the 98 cases revealed the following data: Tuberculosis of the kidney occurs less frequently in the western part of the United States than elsewhere. The rate of survival in patients with renal tuberculosis was lower when active tuberculous lesions were observed in other organs. Stone occurred in 7 cases of renal tuberculosis, cancer in 3 cases and renal hypertension in 3 cases. The rate of mortality following nephrectomy for unilateral tuberculosis in the 81 cases of this type was 1.2 per cent.

Postoperative cystoscopic examination and treatment should be carried out, because of the frequent occurrence of ulcers of the bladder and stricture of the intramural portion of the remaining ureter. Strictures occurred in 28 of the 81 patients operated on. Patients given cystoscopic examination and treatment after operation showed a higher rate of survival than those who received no postoperative care. This observation emphasized the importance of not abandoning the patient after nephrectomy for tuberculosis of the kidney.

*Artificial Kidney.*—Kolff,[10] in an extensive monograph, describes his work on the artificial kidney, which is used in an effort to remove the products of the catabolism of proteins from the body.

As early as 1913, Abel, Rowntree and Turner were able to remove products of catabolism from the blood of animals in experimental studies by means of dialysis. The blood was prevented from clotting and flowed outside the body through a system of dialyzing tubes. The substances with small molecules, to which nearly all the products excreted with normal urine belong, can be removed by dialysis, whereas substances which have large molecules, such as proteins, cannot pass through the membrane.

10. Kolff, W. J.: The Artificial Kidney, Kampen, Holland, J. H. Kok N.V., 1946.

In spite of some later efforts, vividialysis has not found a place in clinical usage. At present, investigators have greater opportunities than earlier workers, because excellent dialyzing membranes (cellophane) and a reliable nontoxic anticoagulation preparation (heparin) are at their disposal.

It was first necessary to construct a dialyzer of sufficient capacity for clinical use. A good dialyzer must spread a small quantity of blood over a large surface; the blood must circulate in a closed system, and the blood as well as the washing liquid must be kept in continuous movement.

After many earlier endeavors, briefly described in his book, an artificial kidney was constructed which is suitable for clinical use. Detailed reports of the first 15 patients who were treated with the artificial kidney have been published in the Dutch edition of Kolff's book. The experience in using the artificial kidney in a clinic has been analyzed as much as possible; the mistakes have been described with a hope to discovering ways for making uninterrupted vividialysis possible. Later treatments took place practically without technical interruptions. Since molecules go both in and out through the dialyzing membrane, much attention has been paid to the composition of the rinsing liquid, as in no circumstances should the patients be demineralized. On the contrary, the mineral spectrum of the patients must be made as close to normal as possible by means of dialysis.

At present a standard rinsing liquid is used for all patients, the results of which seem to give satisfaction; the solution contains 0.6 per cent sodium chloride, 0.2 per cent sodium bicarbonate, 0.04 per cent potassium chloride and 1.5 to 3 per cent dextrose. The concentration of the minerals, potassium, sodium and chloride, and the alkali reserve were closely observed during dialysis.

Continuous dialysis is carried out in which the blood coming from the radial artery flows only once through the artificial kidney and is then brought back into a vein. The blood, which flows once through the kidney, has almost entirely lost its urea and other products of retention. The largest quantity of urea removed in one period of dialysis amounted to 260 Gm.

Other products of retention were also removed. Kloff has been able to prove this for the residual nitrogen, creatinine, uric acid, indoxyl, xanthoprotein and several chemotherapeutic drugs. The clinical phenomena of uremia disappeared within twenty-four hours after treatment was begun, except in those cases in which the artificial kidney was used for a dying patient who did not regain consciousness.

Chronic nephritis is not an indication for treatment with the artificial kidney, although an acute exacerbation of chronic uremia might be an indication in some cases.

Acute uremia, whatever the cause may be, is an indication for treatment with the artificial kidney as soon as it immediately threatens the patient's life.

Some patients become uremic because of anuria or oliguria. Others become uremic even though diuresis of about 1 or 2 liters a day occurs, but the concentration of the urine is bad. This condition may obtain both in patients suffering from acute glomerulonephritis and in patients after operations.

When acute uremia is present the treatment should not be postponed until the general condition of the patient suddenly declines. Kloff came to the conclusion that when acute uremia exists the patient nearly always dies unexpectedly, whereas a short time before death he still makes a good impression clinically.

Kloff proposes to treat the patient with the artificial kidney as soon as the urea content of the blood increases to more than 350 mg. per hundred cubic centimeters (3.5 Gm. per liter) and before that if the potassium content of the blood is higher than normal or if the alkali reserve is too low.

If this is done, the urea content of the blood can easily be brought to less than 100 mg. per hundred cubic centimeters in one period of dialysis. In 1 case the urea content was reduced to 46 mg. per hundred cubic centimeters.

It is now possible to free a seriously ill patient of his uremia in one period of dialysis, which lasts from ten to fourteen hours, so that, after the dialysis, he will have several days' respite before intoxication endangers his life again. In this interval there is a chance that the patient's own kidneys will take up excretion again.

This result occurred in 6 of the 15 patients, 1 of whom survived; the others died from complications.

*Miscellaneous Data.*—Sweetser,[11] in discussing the surgical approach to renal and retroperitoneal tumors, states that surgical treatment for any mass in the kidney or retoperitoneal tissues should be undertaken with recognition of the possibility of malignant disease and with adequate preparation and draping of the field. Since the presence of a malignant lesion is often questionable, exploration is begun through an oblique incision in the flank, and only when a malignant lesion is demonstrated is the incision extended. The incision described by Sweetser preserves the nerve supply of all the abdominal muscles. The unopened peritoneum helps in control and retraction of the intraperitoneal organs and protects them from infection and from damage by evaporation and by trauma of packs and retractors. The lateral posture of the patient

11. Sweetser, T. H.: The Surgical Approach to Renal and Other Retroperitoneal Tumors, J. Urol. **57**:651-659 (April) 1947.

and the shape of the flap result in better exposure than any other approach, because the abdominal contents drop away toward the opposite side, with little or no need for retractors, and the region of the renal vascular pedicle comes well up into the wound for accurate and adequate primary treatment.

Kreutzmann [12] reports 2 cases of hypertension due to solitary renal cyst. In both cases a persistent drop in pressure occurred after destruction of the cysts. A review of the literature on hypertension due to unilateral renal disease revealed 54 cases in which blood pressure was normal one to five years after surgical intervention. The data necessary to the urologist before a decision is made as to whether to operate on a patient are enumerated.

Barker and Braasch [13] made an analysis of 61 cases of hypertension in which advanced unilateral renal disease was observed and in which the affected kidney was removed as treatment for the hypertension.

Follow-up studies in this group of cases have shown that two years after nephrectomy results were good in 25 cases (41 per cent), fair in 10 (16.4 per cent) and poor in 20 (33 per cent) and that 6 patients (10 per cent) were dead.

The condition of 32 patients was followed for five years. At the end of that time, good results were present in 10 cases (31 per cent), fair results in 5 (15.6 per cent) and poor results in 11 (34.4 per cent) and 6 patients (19 per cent) were dead.

Both good and poor results were noted among patients in different age groups, in both sexes and among patients who had hypertensive disease of various degrees of severity.

Clinical analysis of these cases, from the standpoint of the hypertension, failed to reveal information which was of value in preoperative prediction of the effect of nephrectomy on the subsequent course of the hypertension.

No specific urologic or pathologic observations were noted in the affected kidneys removed which would indicate whether good or poor results would follow nephrectomy.

Morrissey [14] discusses the conservative treatment of renal and ureteral colic. In a series of 37 cases of renal and ureteral colic due to stone and of 69 cases in which the colic was caused by obstruction, the administration of "donnatal" (an antispasmodic sedative containing

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12. Kreutzmann, H. A. R.: Hypertension Associated with Solitary Renal Cyst: Report of Two Cases, J. Urol. **57**:467-472 (March) 1947.

13. Barker, N. W., and Braasch, W. F.: The Course of Hypertension After Nephrectomy for Advanced Unilateral Renal Disease, Surg., Gynec. & Obst. **84**:299-304 (April) 1947.

14. Morrissey, J. H.: Conservative Treatment of Renal and Ureteral Colic, J. Urol. **57**:635-641 (April) 1947.

phenobarbital and belladonna alkaloids) was an effective treatment in the relief of pain and spasm; relief occurred in the greater proportion of cases in thirty-six hours. In 197 cases, 'donnatal" was employed to ameliorate the discomfort and spasm following cystoscopy and ureteral catheterization (with or without pyelograms). Reactions were controlled thoroughly when "donnatal" was administered before and after the procedure, reducing the necessity for the use of opium derivates to a minimum. In 45 cases of spasm of the vesical neck (including 9 cases of stricture of the urethra and chronic granular urethrism in women), "donnatal" was used liberally for forty-eight hours after operation, with good results. In 7 cases of cardiospasm in which patients complained of varying degrees of regurgitation substernal discomfort and dysphagia, "donnatal" proved highly efficacious in relieving symptoms. In Morrissey's experience, the range of action of "donnatal" is superior to that of atropine alone and it is more dependable and less toxic than the synthetic preparations.

Bondy and Barnwell [15] present a case of chronic typhoid pyonephrosis and review the literature. Chronic unilateral asymptomatic pyonephrosis caused by Eberthella typhosa occurs rarely and is responsible for certain urinary typhoid carriers. There has been no mortality directly associated with this condition in the reported cases, and the prognosis for cure of the carrier state by nephrectomy is excellent. It is desirable that all urinary typhoid carriers be studied by modern urologic methods, so that patients whose disease is amenable to surgical treatment may be offered its benefits.

Barquin [16] states that according to his technic perirenal insufflation of air no longer is a dangerous procedure. The main purpose of this procedure is to obtain better visualization of the outlines of the kidney and adrenal glands. By means of the lateral roentgenogram he visualizes the anteroposterior diameter. In sclerolipomatous perinephritis he obtains a thick irregular outline of the kidney. A second roentgenogram, taken twenty-four hours later, will disclose more satisfactory diffusion of the gas in the perirenal space. The case which he reports is the second case of sclerolipomatous perinephritis in his experience in which the diagnosis was made with the aid of perirenal insufflation of air alone.

Before operation is performed on a patient who has undergone perirenal insufflation of air, it is wise to wait two or three weeks; otherwise one might encounter dilatation of the capillaries and venous hemorrhage. Barquin states that the sudden deaths observed by some urologists and attributed to gaseous embolism are due to a drop of the

15. Bondy, P. K., and Barnwell, C. H.: Chronic Typhoid Pyonephrosis: Report of a Case, J. Urol. **57**:642-650 (April) 1947.

16. Barquin, F. J.: A New Technique of Perirenal Air Insufflation, J. Urol. **57**:1-14 (Jan.) 1947.

systolic pressure produced during the injection of air by reflex through the sympathetic pathways. This is easily controlled by checking the blood pressure during the procedure.

### URETER

*Neoplasm.*—Kleiman [17] reports a case of metastatic carcinoma of the right ureter, arising from the descending colon, in a 21 year old man.

True metastatic tumors of the ureter are extremely rare. This is believed to be the first reported case of metastatic involvement of the lower part of the right ureter from a lesion in the descending colon.

The degree of surgical treatment depends on whether or not other organs are involved by metastasis.

The prognosis is grave, but early diagnosis and prompt radical surgical treatment can delay the inevitable outcome for a considerable period.

*Stones.*—Ellik [18] discusses the removal of stones from the ureter and their extraction with a looped catheter. He uses the Balkus modification of the Zeiss looped catheter, because the materials needed are readily at hand. He observed that no. 5 F whistle-tipped catheters and no. 32 to 35 steel suture wire were the most adaptable.

Eighty stones were extracted from seventy-two ureters in 71 patients in five and a half months. All except 1 were male patients, and, although the Negro population in naval service was considerable, no stones were encountered in Negroes. Six patients had two stones, 1 patient had three stones and 1 patient had four in one ureter and 18 in the opposite ureter, all of which were extracted. No patient is included whose stone passed spontaneously or after simple manipulation. Thirteen more ureteral calculi have been recently added to the series.

Every stone which could be passed by the catheter and engaged was extracted except one. This was a small stone in the intramural segment of the ureter which could not be passed by again after disengagement. Transvesical ureterolithotomy proved necessary, because of obstruction and infection. Sixteen stones could not be passed by with anything at any time, and operation was performed for ten of these. The remaining six stones were smaller and passed spontaneously after manipulation. All of the stones for which operation was done were in the upper two thirds of the ureter and were large. The majority of the stones were located in the lower segment, but at least 25 per cent were above this level. It was noted that those in the upper part of the ureter responded as well as those near the bladder if the instru-

17. Kleiman, A. H.: Carcinoma of the Right Ureter Secondary to Neoplasm of the Descending Colon, J. Urol. **57**:120-125 (Jan.) 1947.

18. Ellik, M.: Stones in the Ureter: Their Extraction by Looped Catheter, J. Urol. **57**:473-478 (March) 1947.

ment could be passed by them. Stones which fell into the bladder were evacuated or extracted with cystoscopic forceps. Three of these stones, however, were too large for these procedures and required lithotripsy. A large number were delivered through the urethra, into the hand of the operator, still firmly engaged in the loop. Examination of the ureteral orifice, after delivery, revealed little trauma. The urethra was never damaged. Surprisingly little pain was produced by forming the loop or pulling it down the ureter. Stones in the upper part of the ureter seemed to cause slightly more pain than those in the lower segment. Passage through the intramural segment proved the most painful, but was not intolerable. Of eighty-three ureters instrumented, ureteral meatotomy was necessary for only three; the average number of cytoscopic examinations per stone was 1.6, in spite of the fact that impassable stones obviously contributed many cystoscopic procedures to the total figure. Discounting the impassable ones, the stones retrieved averaged 1.4 trials each. No patient was ever subjected to more than five cystoscopic examinations for attempted extraction. One stone was engaged in, and extracted from, the right renal pelvis. Such complications as reflex anuria, infection of the blood stream or renal sepsis were not encountered. Few patients had any pain or fever following the procedure, and in none was cystoscopy repeated for drainage of the instrumented ureter. Chemotherapy was instituted only for the few patients with the febrile reactions.

From this study it would appear that the looped catheter method of extraction of ureteral stones is relatively safe and highly successful. The instrument's small size, ease of passage and freedom from breakable or detachable parts are reassuring. The lack of pain and the few febrile reactions from its use are gratifying. Its presence in the ureter, with stone engaged, aids urinary drainage rather than hinders it. The ureter is unquestionably well dilated by its passage and drains well thereafter. It seems a simple and rather inexpensive instrument and easily replaceable. Its successful use would appear to hinge directly on whether or not a ureteral catheter will pass by the stone or stones present in the ureters. Certainly, with patience and average skill on the part of the user, it promises gratifying results.

*Obstruction.*—Doss [19] discusses the management of obstruction at the ureteropelvic juncture. He states that the excretory urogram offers invaluable assistance as a scout study of the obstructed kidney. Retrograde pyelography is not employed, when the degree of obstruction is advanced, without previous arrangements for continuous drainage of the renal pelvis from the date of cystoscopy to the date of operation.

19. Doss, A. K.: The Management of Ureteropelvic Juncture Obstruction: Translumbar Aortagraphy an Adjunct, J. Urol. **57**:521-538 (March) 1947.

The aortogram assists in determining the "worth" of the kidney, the existence of obstructing aberrant vessels and the importance of such vessels to the over-all renal economy. "Of the procedures employed lateral anastomosis and the Foley-Schwyzer Y plasty have proved most successful." Proper placement of the anastomotic sutures, prolonged splinting of the plastic site and adequate drainage by nephrostomy are indispensable. In a plastic operation on the ureteropelvic juncture, the surgeon should strive for adequate drainage of the pelvis and not anatomic normalcy of the kidney.

Nelson [20] is of the opinion that arteriography is not necessary or advisable as a routine procedure for patients in whom obstruction at the ureteropelvic junction is surmised. Pyelograms are more informative than arteriograms. If arteriography is used for these conditions, there are two pitfalls in reading the arteriograms:

1. The fatty capsule of a hydronephrotic kidney often contains large blood vessels; consequently, in the reading of the arteriogram of such a kidney, the arteries in the fatty capsule must not be mistaken for those in the renal parenchyma.

2. When the radiopaque medium is injected, not all the arteries in the kidney fill simultaneously; therefore, multiple exposures at the intervals of a few seconds are necessary in order to get the correct information as to the supply of blood in the kidney in question.

*Transplantation.*—Higgins [21] discusses transplantation of the ureters into the rectosigmoid for exstrophy of the bladder and reviews 41 cases. He recommends operation during the first year of life for the following reasons: Infants tolerate surgical procedures well. This is evident by the results obtained from other operations, such as those for strangulated hernia, hypertrophic pyloric stenosis and intussusception. As years elapse before operation, recurring attacks of pyelonephritis result in irreparable renal damage, sepsis and, if the delay is great, frequently death. It is probable that the organisms in the intestines of the infant are less numerous and virulent than in older children. Early operation permits normal development from the physical and psychologic standpoints. Operative mortality and morbidity are low. As the child grows older, ureteral obstruction develops at the ureterocystic junction, resulting in dilatation of the ureters, which renders the operation technically difficult and at times impossible. Because of the unfortunate anomaly, the parents become closely attached to the child. Therefore, if death should result from the operation, it is better that it should occur before these ties are well established.

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20. Nelson, O. A., in discussion on Doss,[19] pp. 539-540.

21. Higgins, C. C.: Transplantation of the Ureters into the Rectosigmoid for Exstrophy of the Bladder: Review of Forty-One Cases, J. Urol. **57**:693-700 (April) 1947.

No step of the operation is of more importance than preoperative preparation. This routine, varied with the aged of the child, is advised: (1) liquid nonresidue diet, (2) cod liver oil twice daily, (3) vitamin capsule four times daily, (4) 0.25 Gm. sulfasuxidine (succinylsulfathiazole) per kilogram of body weight every four hours and (5) magnesium sulfate in proportion to age, on the basis that the adult uses 1 ounce (30 cc.) in 8 ounces (240 cc.) of water. On the day prior to operation treatment includes: (1) 10 per cent solution of dextrose by mouth, (2) enemas in the evening until the return is clear, (3) insertion of a mushroom catheter into the rectum two hours before operation to drain off gas, fluids and so forth, (4) administration of tincture of opium, 2 to 8 minims (0.12 to 0.49 cc.), following enemas and once during the night, (5) atrophine sulfate given hypodermically one hour before operation and (6) ether anesthesia. Usually four or five days of hospitalization are required preoperatively, and operation is not performed until the enemas return clear. The operative technic employed is a modification of the Coffey I technic. Simplicity is of paramount importance. In older children both ureters may be transplanted simultaneousy. Higgins has found that better visualization of the operative field and the site of the anastomosis is secured by the intra-abdominal approach, and, therefore, he uses this method rather than the retroperitoneal operation. The operation is performed with the bowl in situ, in order to prevent angulation or kinking of the ureter, a redundant ureter or too much tension on the ureter or line of anastomosis. In this series no peritonitis developed, and with the submucous technic the danger of peritonitis is negligible.

In this series of 41 patients, in whom the ureters were transplanted into the rectosigmoid, 4 postoperative deaths occurred. The remaining 37 patients were dismissed from the hospital in satisfactory condition. Four of them died subsequently. One child died two years after operation, and the cause of death was not determined. The second child died of pertussis complicated by pneumonia three years after operation. One patient died of unknown cause three years after operation. The last patient, in whom the ureter from a solitary kidney was transplanted into the bowel, died of uremia one year after operation.

Davalos [22] reports a new technic of ureterointestinal anastomosis. He states that the main blood supply of the intestine comes from the mesentery and transversely surrounds the intestine; therefore, a transverse cut in the rectosigmoid causes less damage to the blood supply than does a longitudinal incision and the bleeding is minimal. With this transverse incision, it is possible to form a large mucosal flap which acts as a valve and protects the anastomosis against retrograde infection.

22. Davalos, A.: New Technique of Uretero-Intestinal Anastomosis: Further Report, J. Urol. **57**:701-718 (April) 1947.

This flap is formed by the action of the mattress sutures, which, when tied, shorten the intestine in its transverse aspect. The drainage of the ureters is under the direct observation of the surgeon during the entire operation. If the ureters are draining satisfactorily before the mattress sutures are tied, there is no danger of their compression after the sutures are tied. In his belief the following points are of fundamental importance in the success of any ureterointestinal anastomosis:

1. The operative field must be properly exposed by a wide transverse incision with division of the rectus abdominis muscles.

2. The transplantation should be done, whenever possible, intraperitoneally, because both ureters can be transplanted at one operation through the same suprapubic incision, and a site in the sigmoid can be selected for anastomosis which will insure the ureters' remaining permanently in a fixed position.

### BLADDER

*Malignant Neoplasms.*—Jewett [23] states that accurate evaluation of the efficacy of any treatment in the total eradication of primary infiltrating tumors will depend on the exclusion of metastasis and extravesical extension. The clinical application of recent pathologic observations to each patient now permits the exclusion or recognition of metastasis and extravesical extension in a fairly high percentage of cases and indicates the prognosis in most instances. Two general causes exist for low curability: (1) late diagnosis, at which time there usually is extravesical spread, and (2) inefficacy of treatment, which allows a tumor without extravesical spread to persist, often unrecognized, in the bladder wall until it has extended extravesically or has metastasized. Late diagnosis will be avoided only after more complete education of the laity and the members of the medical profession. Inefficacy of treatment will be recognized earlier and more frequently when the importance of an accurate appraisal of the entire pathologic picture is more fully appreciated. The efficacy of different methods of treatment under varying conditions will be demonstrated by the results obtained in the case of potentially curable tumors, that is, in cases in which there is no evidence of local extravesical extension or metastasis.

The cellular appearance of an infiltrating carcinoma of the bladder indicates neither the presence nor the absence of metastasis. However, when the tumor is known to be deeply infiltrating, the poorly differentiated papillary carcinomas have metastasized in nearly half the cases, the poorly differentiated epidermoid carcinomas in at least three fourths and the undifferentiated carcinomas in practically all the cases.

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23. Jewett, H. J.: Infiltrating Carcinoma of the Bladder: Application of Pathologic Observations to Clinical Diagnosis and Prognosis, J. A. M. A. **134**: 496-500 (June 7) 1947.

Accurate diagnosis is established by cystoscopy, biopsy and bimanual palpation.

Recognition of tumor of the bladder usually rests on cystoscopic inspection of the gross characteristics of that portion of the mass lying within range of visualization. Its size, location and margins must be noted. In most cases the lesion is recognized on cystoscopic examination as pedunculated or sessile and may or may not be associated with edema necrosis and ulceration with fibrin or calcareous deposition and hemorrhage.

In questionable cases the diagnosis is established by biopsy, with a properly taken specimen. A good-sized piece of tissue, including some muscularis, should be removed under anesthesia, preferably with a cold rongeur. In the case of pedunculated tumors the piece should be taken immediately beneath the base of the pedicle. In this case a specimen of superficial tissue for biopsy would have led to the diagnosis of benign papilloma, whereas, beneath it, in the wall of the bladder, lay a moderately differentiated epidermoid carcinoma. The inclusion of some muscularis in the properly taken specimen establishes the presence or absence of infiltration as well as the diagnosis of tumor. The clue to the prognosis, however, is not furnished by biopsy alone, for it must be borne in mind that this tissue represents only a relatively small part of the whole tumor. Poorly differentiated carcinomas, when deeply infiltrating, have metastasized in the majority of cases. When they are superficially infiltrating, metastasis from these tumors is infrequent. Carcinomas which appear well differentiated in sections may actually be poorly differentiated in other areas.

With the diagnosis made, and with the infiltration established by biopsy, the next step is to determine the extent to which the tumor has penetrated the wall of the bladder. Since deeply infiltrating tumors in more than 80 per cent of the cases cause stony hard induration and since superficially infiltrating tumors practically never cause stony induration, the clinical segregation of these two groups of cases will depend largely on accurate palpation. In male patients, this is best accomplished rectoabdominally, under anesthesia deep enough to achieve complete muscular relaxation. In female patients, simple pelvic examination usually suffices.

Extravesical extension, with or without fixation, is readily recognized and indicates incurability. Stony induration without evidence of extravesical extension indicates the presence of metastasis in the majority of poorly differentiated tumors and in nearly all undifferentiated tumors. Rubbery induration without extravesical extension denotes a slightly lower incidence of metastasis. In cases of this type, if undifferentiated carcinoma can be excluded, complete destruction or extirpation of the primary growth should result possibly in a higher percentage of cures.

No palpable induration, with the patient under completely satisfactory anesthesia and relaxation, indicates in practically all cases absence of metastasis and, therefore, a high potential curability.

In cases without metastasis and extravesical extension, a good prognosis presupposes complete eradication of the tumor of the bladder and early adequate treatment of future recurrences.

McDonald, Filip and Williams [24] discuss endoscopic treatment of tumors of the bladder. In the treatment of tumors of the bladder by endoscopic means, two main groups of lesions are recognized. The first group consists of tumors that are considered curable. They are nonmalignant papillomas, pedunculated malignant papillomas and small elevated carcinomas, either noninfiltrating or of the early infiltrative type, which possibly have extended only through the mucosa. In the second group are tumors that are not considered curable. They are extensive malignant papillomas, extensive carcinomas and recurrent nodules following previous operative intervention. Treatment in this group is palliative, but, as will be shown, is by no means hopeless. When seen sufficiently early, practically all tumors of the bladder fall into the first group and are curable. Endoscopic removal of the tumor, with wide and deep destruction of the base, is the method of choice in the treatment of these early tumors.

Marshall [25] compares radiation and surgical treatment for cancer of the bladder. He states that there are no five year cures of untreated cancer of the bladder, but approximately 10 per cent of patients may survive five years. On the other hand, 6 per cent of the patients treated with radiation were cured five years after treatment, and 17.3 per cent survived five years. Approximately 90 per cent of patients with untreated cancer of the bladder die within five years, whereas, 80 per cent of the patients treated with radiation were known to be dead in five years. The average survival without treatment was eighteen and eight-tenths months, while the average survival of the group receiving radiation therapy was twenty-four and five-tenths months, compared with a life expectancy in the general population at the same age of approximately fifteen years. All the untreated patients must have died with cancer, although not necessarily of carcinomatosis. In 43 per cent of the necropsies on patients treated with radiation, metastasis was not sufficiently developed to be discovered; this observation indicates that these patients did not die of carcinomatosis. Those with grade 1 or grade 2 malignant lesions survived, on the average, better than did those with grade 3 or grade 4 cancer in the series in which radiation was

24. McDonald, H. P.; Filip, A. J., and Williams, D. C., Jr.: Endoscopic Treatment of Tumors of the Bladder, J. A. M. A. **134**:500-501 (June 7) 1947.

25. Marshall, V. F.: A Comparison of Radiation and Surgery for Cancer of the Bladder, J. A. M. A. **134**:501-507 (June 7) 1947.

used. However, patients with cancer of grades 1 and 2 survived poorly, as indicated by the fact that less than half were known to have survived three years. The fact that a small number of patients who survived ten years, apparently because of radiation, seems to indicate that it is possible for radiation therapy to cure cancer of the bladder, even though such results are uncommon.

Marshall also discusses results of treatment by resection of the bladder and cystectomy and states that it is not assured that the present strong tendency toward surgical intervention will produce decidedly better results than will radiation therapy, but it is unlikely that the results will be worse. Certainly, these results will be better than results obtained without treatment. This investigation does not indicate that radiation therapy should be totally discarded, if for no other reason that that cures have been obtained by its use. Also some pallitation has accrued, mainly in cases of far advanced metastatic lesions. In some instances it probably is advantageous to use both methods of treatment, particularly after the obvious failure of one method. This study seems to indicate that basing the main reliance in the treatment of cancer of the bladder on surgical methods will result, at the least, in a small increase in five years successful results, a moderate improvement in average survival and a really significant amount of palliation as compared with the results obtained by radiation methods.

Priestly [26] discusses the surgical treatment of carcinoma of the bladder. He states that one of the first decisions that must be made before the institution of treatment for a given patient who has a vesical neoplasm is whether a transurethral or a suprapubic approach is preferable. The small noninfiltrating low grade well differentiated lesions are best suited to transurethral treatment. As one's experience with transurethral measures grows, somewhat larger lesions may be treated in this manner. The inherent limitations of this approach, however, always will circumscribe what can be accomplished by this method, and experienced cystoscopists frequently tend to underestimate the extent to which a vesical neoplasm may involve the wall of the bladder. This is due not necessarily to error on the part of the cystoscopist but to the fact that invasion of the vesical wall by carcinoma may occur without visible evidence on the mucosal surface of the bladder. The depth and extent of invasion in the vesical wall can be determined by the cystoscopist only by indirect and somewhat inferential methods. For this reason, it seems safer to err on the side of favoring suprapubic exploration in questionable or borderline types of cases rather than transurethral measures, which time may prove to be inadequate. The details of transurethral treatment are not discussed.

26. Priestly, J. T.: The Surgical Treatment of Carcinoma of the Bladder, J. A. M. A. **134**:507-511 (June 7) 1947.

Of the many details which should be considered in deciding on the most desirable form of treatment for a patient who has carcinoma of the bladder, the following points might be mentioned: the size, location and grade of the lesion, whether it is pedunculated or infiltrating, whether the lesion is single or multiple, the presence or absence of involvement of one or both ureteral orifices, the status of renal function; the existence of serious renal infection, and the age and general condition of the patient. In any case in which a suprapubic operation is performed for vesical neoplasm, intraperitoneal exploration should precede any direct attack on the bladder. The peritoneum should be opened through a low midline incision, and exploration should include the liver and periaoritic and regional lymph nodes as well as the bladder. The extent of perivesical extension and involvement of the peritoneum over the posterior wall of the bladder can be determined with greater satisfaction by transperitoneal exploration than by any other method.

The methods of suprapubic treatment are segmental resection, excision and fulguration, with or without simultaneous implantation of radon, and total cystectomy. Segmental resection is best suited for a growth which is well removed from either ureterovesical orifice, which is situated high in the bladder, either in the dome or on one of the walls, and which is within reasonable limits of size. It is employed usually in treating a patient for an infiltrative type of growth.

Suprapubic excision and fulguration seldom is a procedure of choice in treatment for a vesical neoplasm. This method is reserved for lesions which involve the base of the bladder, including one or both ureteral orifices. In other words, it is employed for a lesion for which total cystectomy usually would be advocated but, for some reason, is not performed. The following types of malignant lesions in the bladder justify exploration with the view to total cystectomy: (1) an extensive low grade lesion which involves most of the bladder, (2) a low grade lesion which involves numerous and diversified regions in the bladder, (3) repeatedly recurring low grade lesion, (4) a high grade infiltrating lesion which, to the best of one's knowledge, can be removed completely by total cystectomy, but probably not by any less extensive procedure and (5) any vesical neoplasm which involves portions of the bladder, such as the vesical neck and ureterovesical orifices, which cannot be removed completely without seriously affecting vesical function. Total cystectomy is being reevaluated and it now is thought that its field of usefulness is broader than has been appreciated in the past. Bilateral ureterosigmoidostomy, which can be performed in most cases of vesical neoplasm, is considered the desirable form of diversion of the urinary flow in association with total cystectomy.

Thomas,[27] in discussing the papers of Jewett,[23] McDonald, Filip and Williams,[24] Marshall [25] and Priestly [26] on urinary vesical tumors, states

27. Thomas, G. J., in discussion on Priestly,[26] pp. 512-513.

that the members of the American Urological Association have expended a large sum of money for the maintenance of a registry so that all tumors of the bladder seen by urologists may be graded and studied. This study has been a group project for many years. Thomas has never been satisfied that the conclusions obtained from this study of vesical tumors was accurate and that the treatment applied was adequate. Many of the bits of tumors that have been sent to the laboratory at the Army Medical Museum have not been removed from that portion of the tumor in which urologists are most interested. Jewett has suggested that bits of muscle fibers should be part of every specimen obtained, as these reveal that the specimen came from the wall of the bladder and not from the top of the tumor. The methods suggested by the assayists make possible an accurate microscopic diagnosis of the presence and extent of the condition. Jewett has alluded to this method of diagnosis of the character of the tumor.

Priestley explores the abdomen when a tumor of the bladder is present. He searches for and determines the extent of local spread or metastasis. Urologists were shunted onto a sidetrack during their treatment of tumors of the urinary bladder with the advent of the transurethral resection. Many undiagnosed tumors of the bladder have been removed and fulgurated transurethrally when segmental resection should have been practiced or complete cystectomy performed.

Thomas states that malignant tumor of the bladder should be attacked as boldly as are malignant tumors of the rectum or of the stomach. If the suggestions that have been made in these papers are followed, one can make an accurate diagnosis of the condition present and can plan a method of attack aimed at the cure of the patient. When suprapubic exploration is made and reveals the presence of cancer of the bladder, without metastasis, the surgeon should be prepared to do (at this time) cystectomy, resection or any other surgical treatment the condition requires.

Lewis,[28] in discussing the papers of Jewett [23] McDonald, Filip and Williams,[24] Marshall [25] and Priestley [26] on urinary vesical tumors, states that urologists have been extremely conservative in the surgical treatment of carcinoma. Yet a radical procedure, such as total cystectomy, should not be employed unless the operation definitely is indicated. Lewis recommends endoscopic treatment for tumors of grade 1 and approves of total cystectomy for extensive infiltrating tumors without evidence of metastasis. There is between these two types, a group of tumors of grades 1 and 2, which tend to recur. Lewis has used total cystectomy for multiple recurrent tumors and has considered adapting radium therapy to meet this problem. The lethal dose for tumor must be

28. Lewis, L. G., in discussion on Priestley,[26] p. 512.

determined and administered. The dose for cancer of the bladder ranges from 8,000 to 12,000 r. Implantation of radon or radium needles means "hot spots" and inadequate total dosage. Roentgen rays produce extensive damage to skin and bowel. The principle he proposes is not new; it is similar to the radium pack. A capsule of 25 mg. of radium is placed in the drainage tube of the Foley catheter, and the balloon is inflated to 35 cc., so that the radium lies at the center of the sphere with a radius of 2 cm. At operation, cystostomy is performed and the tumor is removed or fulgurated. Because 90 per cent of the tumors occur in the prostatic portion of the bladder, irradiation of the tissue bearing the tumor and the site of probable recurrence is accomplished. This method is not satisfactory for deeply infiltrating tumors, but it seems ideal for superficial tumors and for prophylactic irradiation to prevent recurrence. Adequate radiation will kill vesical cancer cells; however, with adequate dosage there must be radium-induced cystitis, which clears in six or eight months. Radium may contribute to the handling of tumors which are not susceptible to transurethral surgical treatment alone and for which the necessity for carrying out cystectomy is doubtful. Lewis states that a radium balloon catheter with adequate drainage facility can be made, so that cystostomy will not be necessary.

Lowsley,[29] in discussing the papers of Jewett,[23] McDonald, Filip and Williams,[24] Marshall [25] and Priestly,[26] states that Marshall has presented statistics in which emphasis has been placed on radiation but surgical procedures also have been done. Marshall says that radiation can cure cancer but does so in only a small percentage of cases, and the general results are only a little bit better as far as life expectancy is concerned than results noted in cases in which no treatment is given. This is a most important observation, coming from the world's greatest center of enthusiasm for radiation. Jewett has called attention to the four causes of failure in any method of treatment. Lowsley heartily agrees with those observations, but he feels that sometimes operation, either cystectomy or even transplantation of ureters to the bowel in hopeless cases, is advisable for the relief of pain, because it is the duty of the physicians not only to "heal the sick but to relieve human suffering." The best results in Lowsley's experience have been obtained by thorough suprapubic excision of vesical tumors, large or small, with a wide cuff of normal wall. The ureter may have to be transplanted to another part of the bladder. Lowsley's first operation of this sort was done in 1918, and this patient is hale and hearty as of the time of writing. This resection should be done regardless of the grade of the tumor if it is accessible and the patient's condition warrants the operation, because Lowsley has had several cases of tumor of grade 1 malignancy in which the

29. Lowsley, O. S., in discussion on Priestley,[26] p. 512.

patients have returned months later with tumors of grade 3 or 4. Following the removal of any tumor of the bladder it is his custom to utilize the Kirwin treatment, which consists of bathing the operative site with 50 per cent solution of phenol in glycerin for a period of three minutes and then with alcohol. This effectively prevents implants. He agrees with McDonald that patients should be followed up and regular cystoscopic examination performed. He advises fulguration of small papillomatous tumors. Painless hematuria should be considered a serious symptom, to be viewed with alarm until its source is discovered. Only in this way will there ever be an opportunity to cure cancer of the bladder, or of any other organ of the genitourinary tract, by operative intervention.

Hinman,[30] in discussing the papers of Jewett [23] McDonald, Filip and Williams,[24] Marshall [25] and Priestley,[26] states that it is remarkable that these four papers all are as much in agreement as they are. The problem of tumors of the bladder is largely one of differential diagnosis and selection of treatment. The problem is changing, however, from what it was a number of years ago. Ten years ago it was estimated that probably 90 per cent of all tumors of the bladder were papillomatous. Of malignant tumors of the bladder, 80 per cent are in persons more than 65 years of age and 90 per cent in those more than 50 years of age. From the years 1930 to 1940, the number of persons more than 65 years old in the United States increased by 35 per cent. The significance of this is that the incidence of cancer of the bladder is increasing.

In differential diagnosis the proper application of four different methods of treatment must be considered: (1) fulguration, (2) irradiation, (3) surgical resection of the local growth and (4) radical cystectomy. The early papillomas and a number of infiltrating papillomas can be cured, but some types of infiltrating tumors cannot be cured by diathermy. The differential point to decide in making the examination is what the treatment will be. Will physicians depend on diathermy or at once adopt some radical procedure? Radium or roentgen radiation may be used. Tumors so located that they can be removed can be successfully treated by this method. In certain cases, however, neither diathermy nor resection can be used, and in them the treatment is total cystectomy with transplantation of the ureters. The important thing in differential diagnosis is to be able to make this decision early. In many cases, total cystectomy is not successful because of the procrastination and delay in instituting this radical procedure. If physicians could decide that the only hope for these patients was in total cystectomy and ureteral transplantation, probably the operation would be performed earlier and more patients would be saved.

30. Hinman, F., in discussion on Priestley,[26] pp. 511-513.

When fulguration is employed, regular periods of reexamination are important. It has been Hinman's custom to have the patient returned a month after the first fulguration and then to destroy any recurrence. If there is no recurrence he returns in two months, then three months and then every three months for a period of two years and then intervals of six months for another two or three years. The patient is usually followed up for at least three years after the last recurrence. Thorough fulguration and deep diathermy cure many papillomatous tumors. They will not cure the sessile flat infiltrating tumors. These tumors have to be cured by either radium therapy or surgical removal. Hinman's experience with irradiation has been disappointing. Many of the patients have suffered a year or more with excruciating burns of the bladder. Not much can be done to relieve them. Practically all vesical tumors are radioresistant. The majority of urologists rely on the other three methods, fulguration, wide resection when possible and, as a last resort, either palliation or radical cystectomy with transplantation of the ureters.

Ritter [31] discusses total cystectomy for infiltrating carcinoma of the bladder and concludes that cancer of the bladder is limited to that organ for a protracted period. The earlier radical cystectomy is carried out, the better the results. Preliminary palliative measures are dangerous. Perineoabdominal cystectomy is less shocking and can be performed comparatively rapidly. Cases must be selected carefully, and the procedure should not be reserved for dying patients. Cure should be expected if the operation is performed prior to the presence of metastatic lesions. Ureterocutaneous anastomosis is not entirely free of complications, but lends itself to a simple rapid operative procedure with ureters under control at all times. Ritter reports 7 cases of total cystectomy with no operative deaths.

Colby and Sniffen [32] present a classification of tumors of the bladder which correlates the cystoscopic and histologic characteristics of these neoplasms. One hundred and thirty tumors of the bladder, not suitable for surgical treatment, were given external radiation with the 1,200 kilovolt unit. Some of these tumors responded well, and others showed little or no response. A histologic study of the tumors gave no clue as to why this was so. Papillary and nonpapillary tumors responded about equally well, and the tumors regressed in a third of the cases. Symptoms were relieved in about half the cases. Colby and Sniffen state that the histologic changes described as "radiation reaction" are in no way typical

31. Ritter, J. S.: Total Cystectomy for Infiltrating Carcinoma of the Bladder, J. Urol. **57**:719-721 (April) 1947.

32. Colby, F. M., and Sniffen, R. C.: Carcinoma of the Bladder: A Classification of Epithelial Tumors and a Study of the Effects of External Radiation, J. Urol. **57**:133-139 (Jan.) 1947.

since they occur before and inconstantly after radiation therapy has been given.

*Inflammatory Conditions.*—Nesbit [33] discusses anterolateral chordotomy for intractable pain resulting from interstitial cystitis. The first patient on whom chorodotomy was done was a woman, 37 years old, suffering from frequency of urination, pain in the bladder on filling and difficulty in voiding. Urologic examination disclosed a typical lesion of interstitial cystitis situated in the dome of the bladder on the right side. The patient was treated by overdistention of the bladder and by instillations of 0.25 per cent solution of silver nitrate into the bladder. This gave her considerable relief for a time, but, eventually, local treatment did not produce a beneficial response and, later, low lumbar sympathetic ganglionectomy and presacral neurectomy were performed. This operation gave immediate relief of symptoms, and she enjoyed normal and comfortable micturition for two and a half months; then all of the previous symptoms returned and suffering became more intense than ever before. Cystoscopy showed a long stellate scar situated at the site previously described. This region bled easily when the bladder was distended. The lesion was slightly fulgurated with the high frequency current. Following the fulguration, she was comfortable for a few days only, but while she was still in the hospital severe pain developed. She was eventually unable to urinate, because of spasm of the sphincter muscle. For two weeks, treatment consisted of drainage with an indwelling catheter and intermittent and later continuous irrigation of the bladder with a weak solution of silver nitrate. The pain became intolerable, and bilateral anterolateral chordotomy was performed at the level of the third thoracic segment of the spinal cord. After operation, she complained of severe and constant pain in the bladder and was relieved of it only after being given large doses of narcotics and sedatives. The pain lasted three weeks. Postoperative dysfunction of the bladder requiring catheter drainage persisted for about a month; the patient then gained complete control of urination and was able to void in amounts up to 250 cc. and empty her bladder, and she was free from pain. At the time of writing, more than two years following operation, she is free from all discomfort referable to the bladder.

The second patient was a man, 24 years old, who had suffered from frequent urination and pain in the bladder on filling for about one and a half years. Cystoscopy under general anesthesia disclosed a small area of typical interstitial cystitis on the left wall of the bladder. The lesion bled freely when the bladder was distended. The urine was free from any abnormality except the presence of red blood cells, and results of

33. Nesbit, R. M.: Anterolateral Chordotomy for Refractory Interstitial Cystitis with Intractable Pain, J. Urol. **57**:741-744 (April) 1947.

inoculations of guinea pigs, as well as cultures of the urine, did not reveal tubercle bacilli. Chordotomy was advised as a preferable procedure and was performed. After operation, the patient was unable to urinate spontaneously and required constant catheter drainage for twenty-one days. During the first two and a half postoperative weeks, he complained of severe and continuous pain in the bladder, pain that was relieved only by heavy narcosis and sedation. After three weeks he was entirely free from pain, urinated spontaneously in normal amounts and emptied his bladder. Eleven months after his operation he was completely free from vesical pain at all times, had normal micturitional behavior and control and no nocturia. He reported that he experienced normal sexual desire, that his sexual function seemed to be entirely normal and that he ejaculated normally.

*Incontinence.*—Bartlett [34] states that when a patient who has stress incontinence is examined in the lithotomy position, the urethra, instead of pointing almost horizontally, usually assumes a nearly vertical direction. This results from a tearing of the layers of pelvic fascia between the bladder and the anterior vaginal wall and the structures of the urogenital diaphragm. Displacement of the vesical neck and urethra impairs the function of the sphincter mechanism and leads to stress incontinetnce. The success of an operative procedure for stress incontinence depends on the replacement of the urethra and vesical neck in their normal positions, by whatever means attained, rather than on the reapproximation of the voluntary muscle fibers.

Bartlett reports the results of operations on 62 patients. All had incontinence, which was believed to have resulted from the trauma of childbirth. Kennedy's technic was employed in the first 42 cases. In this procedure, the vaginal mucosa is elevated from the vesical neck and posterior two thirds of the urethra and the dissection is carried laterally under the pubic rami until the urethra is entirely freed of its lateral attachments, including any post-traumatic scar tissue that may be present. Kennedy stated that the formation of bands of scar tissue between the urethra and pubic rami laterally is a factor in the impairment of function of the voluntary sphincter. The urethra is then plicated in the midline to restore the function of the involuntary sphincter. In Bartlett's last 21 cases, stripping of the lateral attachments of the urethra from the pubic rami was not done. Cures are reported in 71 per cent or 15 of these 21 cases. In Bartlett's technic, a longitudinal incision is made in the anterior vaginal wall and the mucous membrane is elevated. Dissection is carried laterally, close to the mucosa, and a good avascular plane is encountered which may be

34. Bartlett, M. K.: The Surgical Treatment of Urinary Incontinence, New England J. Med. **236**:965-969 (June 26) 1947.

easily followed laterally to the pubic rami. The pelvic fascia is revealed as a smooth glistening layer, and, as the dissection is carried anteriorly toward the external meatus, the region of the urogenital diaphragm is exposed. The pelvic fascia and urogenital diaphragm are then approximated over the urethra and the neck of the bladder and then infolded by a second row of sutures. The mucous membrane is then closed. Various types of suture material were used. Surgical gut seemed to be the best, perhaps because of a greater inflammatory reaction with more formation of scar tissue.

Ormond [35] discusses treatment of stress incontinence in women and describes Kennedy's method. A Foley catheter is inserted into the urethra, and the bag is inflated. This is to facilitate recognition of the neck of the bladder. The cervix is grasped with a tenaculum, and the vaginal wall is incised along the urethra from shortly behind the meatus to well beyond the vesical neck. Then by blunt dissection close to the rami of the pubis, with the handle of the knife or a Kuttner dissector, the urethra is dissected free from the ramus on each side. This dissection must be done gently, with strokes directed medially. It is necessary to keep close to the bone to avoid a plexus of veins and branches of the inferior vesical artery, and the dissection must extend well about the vesical neck into the paravesical space. As it is done, the breaking of the fine adhesions between the urethra and the rami can be felt, and freedom of motion of the urethra and internal sphincter is restored. In order to maintain this freedom of motion, the tissues under the urethra are plicated by three mattress sutures; the posterior suture is similar to the old Kelly stitch. Then another row of mattress sutures brings together over the first row of sutures the tissues on each side of the urethra and the edges of a fascia-like structure that lies there.

Any redundancy of the vaginal wall is then removed, and, if there is no appreciable redundancy, a strip is cut from each vaginal flap in order to remove whatever damaged portions of the voluntary sphincter there may be. Then the remaining fibers of this muscle are brought together beneath the urethra with three chromic surgical gut sutures. These sutures are passed through the vaginal wall close to the rami to insure picking up the fibers of the voluntary sphincter. Silver wire may be used. A catheter is left in place for a few days. Kennedy warns that a factor such as infection or hematoma beneath the restored urethra may dissolve the plicating sutures and may cause failure by allowing the urethra to resume to some extent its preoperative position. He recommends free drainage of the paravesical spaces and leaving the flaps of the vaginal wall open.

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35. Ormond, J. K.: Treatment of Stress Incontinence in Women, J. Urol. **57:** 326-330 (Feb.) 1947.

*Miscellaneous Data.*—Nesbit and his associates [36] discuss the effects of blockade of the autonomic ganglions. They state that parenteral administration of the tetra-ethyl ammonium ion produces an impairment in the ability of autonomic ganglions to transmit nervous impulses. A study was made of the effects of tetra-ethyl ammonium bromide on the urinary bladder and the act of micturition. Thirty patients were examined by the cystometric method, before and after the administration of tetra-ethyl ammonium bromide; an average dose of 500 mg. was used. Of the thirty bladders sixteen were normal, three autonomous neurogenic, five unihibited neurogenic, three reflex neurogenic and three were miscellaneous types of neurogenic bladders.

Seventy-five per cent of the normal bladders demonstrated a partial or complete response to tetra-ethyl ammonium bromide. A complete response is arbitrarily designated as one in which the voiding contraction of the detrusor urinae muscle is abolished and the patient is unable to void. A partial response is one in which the amount of urine and the capacity of the bladder are greatly increased. The autonomous neurogenic bladders demonstrated no change in the cystometrogram after the administration of the tetra-ethyl ammonium ion. The drug abolished both the uninhibited and the voiding contractions of the detrusor muscle in four of the uninhibited neurogenic bladders and the uninhibited contractions in the fifth bladder. All of these bladders showed a decided increase in capacity. The reflex neurogenic bladder and two bladders of miscellaneous type demonstrated responses to tetra-ethyl ammonium bromide. Visceral sensation in all the bladders was totally unaffected by the drug. The ability of the bladder to maintain an approximately constant intravesical pressure with varying volumes of fluid was not abolished by parenteral administration of the tetra-ethyl ammonium ion.

Emmett [37] discusses the management of cord bladder by transurethral resection. During 1944 and 1945, at the Mayo Clinic, 45 patients suffering from cord bladder underwent transurethral resection. Thirty of these patients had transverse lesions of the spinal cord, resulting from either trauma or inflammatory disease. The remaining 15 were suffering from various lesions of the spinal cord, such as multiple sclerosis and combined sclerosis.

The causative factors in 30 cases in which transverse lesions of the spinal cord were present were (1) trauma, (2) inflammatory myelitis,

36. Nesbit, R. M.; Lapides, J.; Valk, W. W.; Sutler, M.; Berry, R. L.; Lyons, R. M.; Campbell, K. N., and Moe, G. K.: The Effects of Blockade of the Autonomic Ganglia on the Urinary Bladder in Man, J. Urol. **57**:242-250 (Feb.) 1947.

37. Emmett, J. L.: Further Observations in the Management of Cord Bladder by Transurethral Resection, J. Urol. **57**:29-41 (Jan.) 1947.

(3) postoperative sequelae of tumors of the spinal cord and (4) effects of previous administration of a spinal anesthetic agent.

Urologic examination of the 30 patients yielded interesting results. Excretory urograms were made in 17 cases. In 4 the urograms showed evidence of bilateral pyeloureterectasis; in 1 there was evidence of unilateral ureterectasis, and in 12 there was nothing abnormal. All patients had residual urine; the amount varied from 50 to 1,200 cc. The amount was 100 cc. or more in all but 2 cases.

The object of transurethral resection in this type of case is to remove or destroy the capacity of the vesical neck or internal sphincter to contract and to remove any adenomatous or obstructing prostatic tissue, so that there will be no resistance between the bladder and the external urethral sphincter. To do this, the surgeon must resect the entire circumference of the vesical neck and then carry the resection well out to the verumontanum. If the external sphincter is not damaged, incontinence should not occur. In a large proportion of cases operation must be done in two stages. In occasional cases, even in experienced hands, a third or even fourth resection will be necessary before the patient can empty his bladder completely. In 23 cases the results were considered good; in 4 the condition of the patients was improved; in 2 results were fair, and in 1 case the result was poor.

The miscellaneous lesions in the second group (15 cases) were as follows: multiple sclerosis in 7 cases, combined sclerosis in 4, diabetic neuritis in 1 case, degenerative lesion of the spinal cord in 1 and arachnoiditis in 2 cases in which exploratory operation had been performed previously.

Emmett states that the performance of transurethral resection by no means eradicates or treats the underlying cause of the disability, namely, the neurologic lesion; rather, a mechanical defect is corrected and the patient is taught to substitute the use of intact muscles for the use of muscles that are paralyzed. In the final analysis, an effort is being made to eliminate residual urine, in order to allow the patient to remain dry from the time the bladder is emptied until an amount of urine equal to that of the previously carried residual urine reaccumulates in the bladder. It is obvious that abdominal muscles and the diaphragm are of great importance, because if they are intact the patient will be able to exert considerable abdominal pressure to help empty the bladder. Manual compression is also important in this respect. When the neurologic lesion is situated higher in the spinal cord, however, so that the abdominal muscles are paralyzed, a more efficient type of reflex or automatic bladder often results, which may more than compensate for the intact abdominal musculature present when the injury is situated lower in the spinal cord.

*Chanages in the Vesical Neck.*—Pereira [38] states that filling of the urethrocystogram enables one to distinguish the structure of the normal neck from its pathologic changes. It verifies neatly and definitely the presence of the "disectasias" of the neck and portrays each type of "disectasia" and the various signs of vesical dysfunction. It identifies each of the clinical types of the adenoma of the prostatic urethra (miniature type, median lobe, ventral lobe, lateral lobes, total adenoma), as well as other modes of development (vesical, subvesical), permitting a better choice of the method of treatment (suprapubic, perineal operations, endoscopic resection). It demonstrates, on the other hand, that, in growing, the adenoma does not invariably flatten the prostate gland against Denonvilliers's fascia, changing it into the so-called surgical capsule. The gland also may remain untouched below the adenoma itself. It brings to light signs of malignant prostatic tumor after it has progressed considerably. Finally, it permits the verification of postoperative developments and complications (structural deformities), which delay clinical recovery of patients operated on for "disectasias" of the neck, adenoma and cancer of the prostate gland.

*Rupture.*—Oppenheimer and Druckerman [39] discuss recurrent nontraumatic intraperitoneal rupture of the urinary bladder and report a case.

When no external trauma or internal instrumental assault has occurred, the rupture may be arbitrarily designated as nontraumatic or as spontaneous perforation. Ruptures may be intraperitoneal, extraperitoneal or mixed types. The extraperitoneal variety is the least dangerous. The mortality rate from intraperitoneal rupture has been high because operation is often delayed in the attempt to ascertain the cause of the early signs of peritonitis.

Obvious predisposing factors to nontraumatic rupture are as follows: (1) a bladder weakened by distal obstruction of long standing, (2) sudden increase in the intravesical pressure, as an act of difficult urination or the lifting of a heavy object, in the presence of a distended or overdistended bladder and (3) inflammatory, infectious, vascular, neoplastic, degenerative or other disease of the bladder.

### TESTIS

*Neoplasm.*—Taylor [40] reports 3 cases of testicular tumors. The first case is one of bilateral seminoma in which cure has lasted more than

38. Pereira, A.: Some Information Derived from the X-Ray Examination of the Neck of the Bladder and of the Prostatic Urethra, J. Urol. **57**:1054-1068 (June) 1947.

39. Oppenheimer, G. D., and Druckerman, L. J.: Recurrent Non-Traumatic Intraperitoneal Rupture of the Urinary Bladder: Recovery, J. Urol. **57**:238-241 (Feb.) 1947.

40. Taylor, J. A.: Three Cases of Testicular Tumor, J. Urol. **57**:175-184 (Jan.) 1947.

nineteen years from the time of the first orchidectomy and fourteen years from the second. The second case is one of bilateral testicular tumors, a teratoma on the left and a seminoma on the right, both of which have metastasized; the cure in this case has lasted more than fourteen years from the time of the first orchidectomy. The third case is one of chorionepithelioma in which cure has lasted nine years.

*Orchidopexy.*—Vermooten [41] discusses orchidopexy and presents a new modification of the Bevan technic.

The incision is usually 10 cm. long. It begins just lateral to the pubic tubercle, extends upward and outward to a point 4 cm. medial to the anterior superior iliac aspect of the spine and exposes the aponeurosis of the external oblique muscle. This is divided in the direction of its fibers upward from the center of the external inguinal ring. The internal oblique muscle is then retracted medially; the spermatic funiculus is lifted up from its bed and freed downward, and the gubernaculum is divided. The processus vaginalis is then opened, the testis is located and the sac opened up to the internal ring. Just before reaching the internal ring the sac is cut across, and, in so doing, care is exercised in separating the thin peritoneum from the spermatic vessels and the vas, for it is intimately adherent to these structures, particularly if nature has attempted to obliterate the sac in this region, as so frequently happens. When a hernial sac has developed, the vas is dissected down the lateral abdominal wall and the spermatic vessels are dissected as high as possible. The hernial sac may now be closed by a purse-string suture of no. 0 chromic surgical gut or no. 20 cotton, or, if preferred, it may be opened into the potential direct sac by the Houget maneuver and the new sac thus formed closed with no. 20 cotton or no. 0 chromic surgical gut.

After the actual or potential congenital hernial defect is disposed of, attention is directed to the lengthening of the cord, the first essential of which is to separate the vas and its accompanying vessels from the spermatic vessels by blunt dissection, in this way removing the remainder of the processus vaginalis from the cord. Fibrous bands which prevent the adequate lengthening of the cord are now divided until such time as the cord is long enough to permit the testis to be placed in the bottom of the scrotum with little, if any, tesion. If the vas is too short and so prevents adequate length being obtained, it may be divided, for except in bilateral cases there is no real objection to sacrificing the spermatogenic function of a testis which may in the normal course of events never have such function. However, if adequate length cannot be obtained because of too short a vascular pedicle, orchiectomy should be done.

41. Vermooten, V.: Orchidopexy: A New Modification of the Bevan Technique, J. Urol. **57**:310-318 (Feb.) 1947.

Anatomically, the scrotum is filled with elastic connective tissue fibers, and these fibers cannot be separated adequately with one finger to obtain a good bed for the testis. A better bed can be made with two fingers of one hand, but even then the majority of elastic fibers cannot be adequately separated. If both index fingers are used, a still better bed can be made. Vermooten has observed that, in order to obtain a bed which will permit the testis to remain in the bottom of the scrotum, the remaining elastic fibers must be divided with a knife. After what appears to be an adequate bed has been made, the most dependent portion of the scrotum is grasped with a sponge-stick and invaginated into the wound. The elastic fibers are then incised over the sponge-stick and pushed off away from it with a piece of gauze, until only the skin, with no underlying subcutaneous fascia, is present in the wound. The scrotum is now invaginated, and two fingers are introduced to separate further the elastic fibers. When a large enough space has been made to accommodate the testis, the scrotum is again invaginated with the aid of a sponge-stick. An anchoring suture of no. 0 chromic surgical gut is passed through the mesorchium or through the remnants of the gubernaculum. With each end of the suture on a long straight needle, the needles are passed, one on each side of the sponge-stick, through the scrotum. When this suture is tied on the outside of the scrotum, the testis is automatically fixed in the most dependent portion of the scrotum. The wound is now closed by suturing the internal oblique muscle and conjoined tendon to the shelving edge of the ilioinguinal ligament; this suturing buries the cord. The aponeurosis of the external oblique muscle is imbricated over this with interrupted sutures of no. 0 chromic surgical gut; Scarpa's fascia is approximated with a few interrupted sutures of no. 00 plain surgical gut, and the cutaneous edges are approximated with cotton.

Traction is now applied to the testis and the scrotum by the aid of an elastic band to the medial aspect of the opposite thigh.

## PENIS

*Peyronie's Disease.*—Lowsley and Gentile [42] report a series of 27 cases in which operation has been performed for Peyronie's disease and conclude that the disease occurs in every decade of adult life from the third through the seventh. If operation is done sufficiently early, cure can be obtained in a large majority of cases. Better results are obtained in younger patients than in older patients.

The technic of the operation has been improved by inserting a pad of fat to bring about hemostasis and by not approximating Buck's fascia,

42. Lowsley, O. S., and Gentile, A.: An Operation for the Cure of Certain Cases of Plastic Induration (Peyronie's Disease) of the Penis, J. Urol. **57**:552-562 (March) 1947.

but merely compressing the fat with the suture. The disease may manifest itself by ventral or downward flexion of the penis in rare instances. In these cases operation does not result favorably.

### GENITOURINARY TRACT IN GENERAL

*Drainage and Irrigation.*—Deming [43] states that the present or modern concern for drainage and irrigation of the urinary tract has extended beyond making the patient comfortable and includes consideration for biocellular response and the prevention of the development of further pathologic conditions in the vital organs. Much wasted energy and effort have been utilized in inventing noiseless and complicated types of apparatus. The use of the Fenwal flask with irrigation with an isotonic solution of sodium chloride is recommended as the least troublesome and the most economical irrigating apparatus. The irrigating fluid of isotonic solution of sodium chloride maintains a clean mucous membrane surface, without inhibiting the natural defense mechanism of the cells to infection. Henry Morton's advice, with regard to preserving the space of Retzius intact, is to be commended. The use of T tube drainage of the ureter is a distinct advantage in giving adequate drainage without the development of ureteral fistulas. Nephrostomy is at times the best renal drainage, but, for patients suffering from staghorn calculi with infection, postoperative drainage with two urethral catheters, associated with constant irrigation with an isotonic solution of sodium chloride has given excellent results. Future progress in renal surgical treatment lies in conservation of the functional tissues by preventing ischemic areas without having to make incision into the kidney or allowing infection to occur.

*Familial Eunuchoidism.*—Roth [44] presents 4 cases of eunuchoidism in brothers; the hypogenitalism was associated with other ectodermal and mesodermal defects to produce an incomplete form of the Laurence-Moon-Biedl syndrome. The family tree showed questionable parts of the syndrome in several antecedents and transmission of obesity through a female sibling.

Testicular biopsy and androgenic and gonadotrophic assays of the urine are reported in this syndrome. The testicular condition seen in the 4 cases was the result of anterior pituitary failure. Androgenic activity of the adrenal glands was thought to be impaired and was also considered as secondary to lack of anterior pituitary stimulation. Replacement therapy with testosterone produced an increase in muscu-

43. Deming, C. L.: Modern Conception of Drainage and Irrigation of the Urinary Tract, J. Urol. **57**:49-60 (Jan.) 1947.

44. Roth, A. A.: Familial Eunuchoidism: The Laurence-Moon-Biedl Syndrome, J. Urol. **57**:427-442 (March) 1947.

lar tone, and this, in turn, modified signs which are usually associated with neurologic disease. For this reason, Roth expressed the opinion that the muscular hypotonia resulting from lack of adequate amounts of androgen was productive of these signs.

The prevailing views concerning the genetic aspects of the Laurence-Moon-Biedl syndrome and familial eunuchoidism are presented.

Also reported is the case of a Negro who had an incomplete form of this syndrome without hypogenitalism.

Chute,[45] in discussing Roth's paper, reported on the original article by Laurence and Moon in the *Ophthalmic Review* for 1886, in which they described the observations in the 3 brothers, all in their teens, and in their little sister. These patients were short, heavy and flabby and had a tipsy dragging gait, pigmented degeneration of the retina and reduced intelligence. The boys all had infantile external genitalia, with a few scattered pubic hairs. The girl (aged 7 years), who was not examined as thoroughly as the boys, was said by her mother to have normal sexual development for her age.

This so-called syndrome does not represent a disease entity, but is a rare combination of more or less heredofamilial characteristics, as shown by the fact that in most cases in which the condition is classified as belonging to the Laurence-Moon-Biedl syndrome the patients do not have the exact classic combination of signs; many have too few, and some have too many. Thus, the 4 brothers, whose cases were reported by Roth, lacked a number of the traditional features. Although they had degeneration of the retina, none of them had retinitis pigmentosa, they did not have polydactylism or mental deficiency, they were not short and only 1 was decidedly obese.

The modern methods of diagnosis used, testicular biopsy and measurements of the seventeen ketosteroids and of the gonadotropins in the urine, are dispelling somewhat the mystery which used to surround this type of disease and are revealing more of what is actually going on physiologically. Thus, it is now possible to determine whether the anterior pituitary gland or the testes are primarily at fault and, also, whether merely the tubular spermatogenic function of the testes is deficient or the Leydig interstitial cells also fail. Accurate diagnosis of the condition present is a guide to intelligent and successful treatment.

*Urinary Stone.*—Prien and Frondel[46] state that the analysis of urinary calculi by chemical methods is unsatisfactory. Many supposed constituents of calculi recorded in the medical literature are found to be nonexistent when sought by modern physical methods of identification.

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45. Chute, R., in discussion on Roth,[44] pp. 443-445.

46. Prien, E. L., and Frondel, C.: Studies in Urolithiasis: I. The Composition of Urinary Calculi, J. Urol. **57**:949-991 (June) 1947.

All urinary calculi are crystalline. Therefore, they should be amenable to analysis by the modern physical technics used in the study of minerals. These methods include the use of polarized light (optical crystallography) and roentgen ray diffraction photography (roentgen ray crystallography).

In routine analysis, the calculi are first fractured and dissected with a pointed tool under low magnification with ordinary light. Samples of material are carefully selected from the nucleus, various layers and so forth, powdered and identified under the polarizing microscope. Optical analysis is simple, rapid, approximately quantitative, rigorously accurate and applicable to all calculi, including those of microscopic size. The crystalline components of urinary calculi are: calcium oxalate monohydrate, calcium oxalate dihydrate, magnesium ammonium phosphate hexahydrate, carbonate-apatite and hydroxyl-apatite, calcium hydrogen phosphate dihydrate, uric acid, cystine and sodium acid urate. Calculi of pure calcium oxalate constituted 36.1 per cent of the total; mixed calculi of calcium oxalate and apatite comprised 31.0 per cent; together they composed 67.1 per cent of the total. These calculi usually occur in acid sterile urine. Calculi of pure magnesium ammonium phosphate hexahydrate, pure apatite and mixed magnesium ammonium phosphate hexahydrate and apatite comprised 19.5 per cent of the total. These calculi usually occur in alkaline infected urine. Calcium hydrogen phosphate dihydrate occurred in 1.6 per cent of the calculi. Uric acid and cystine exist more frequently in pure than mixed form and occurred in 6.1 per cent and 3.8 per cent, respectively, of the calculi. Sodium acid urate occurred but once in the series and in microscopic amount. It was the only urate observed.

*Periurethral and Perirectal Infection.*—Tashiro and Hinman [47] studied the clinical similarity of periurethral and perirectal infections and their pathologic and clinical differentiation. They state that in their experience periurethral phlegmon and far advanced perirectal abscess frequently have not been differentiated before operation. The site of greatest swelling, tenderness and fluctuation may be the same, and the systemic manifestations are similar (malaise, fever, chills, toxemia, icterus, prostration, dehydration and pain on urination and defecation, with a "bearing down sensation" in the pelvis).

It is important to differentiate between these diseases preoperatively, because the surgical treatment differs in important respects. In extravasation of urine (septic or sterile) the necessity for immediate cystostomy in addition to radical incision is emphasized, whereas spreading perirectal infections demand adequate and often extensive incision and drainage but cystostomy may not be indicated.

47. Tashiro, S., and Hinman, F., Jr.: Periurethral and Perirectal Infections: Pathological and Clinical Differentiation, J. Urol. **57**:338-355 (Feb.) 1947.

Tashiro and Hinman review 7 cases of perineal infection and state that anatomic continguity is an important factor in the similarity of signs and symptoms. The fascial barriers, which are effective against uninfected urine, may fail to limit the phlegmonous process of inflammatory urinary extravasation. Neither are they proof against pus under pressure in the ischiorectal and other perirectal spaces.

*Cystoscopic Reactions.*—Lewis [48] states that cystoscopic reactions may be classified into two groups: (1) a local type in which ureteral colic is the prime symptom and (2) a systemic type which presents a picture of sepsis. Local reactions may be eliminated by sedation, gentleness and avoidance of overdistention of the renal pelvis. Administration of 1 Gm. of sulfathiazole every four hours to patients undergoing reactions will reduce the morbidity of this complication by several days. Systemic reactions are almost entirely eliminated by the administration of sulfathiazole (1 Gm. four times a day) for five days, during which time cystoscopy is conducted. The status of a patient, whether ambulatory or bedfast, the type of examination, be it pyelography or simple cystoscopy, and the duration of instrumentation had no bearing on the incidence of reactions. Prostatitis following cystoscopy may be expected in more than half of all cases unless sulfathiazole is used. Reactions were commonest when prostatitis was developing, although they occurred in a milder form when prostatic leukocytosis was not demonstrable. Severe reactions were three times as frequent when prostatitis was present, whereas when reactions occurred in the presence of normal cell counts in the urine they were more likely to be mild. Administration of 1 Gm. of sulfathiazole four times daily for five days, beginning on the day prior to cystoscopy, will not only eliminate 91 per cent of all reactions but also will reduce the incidence of postcystoscopic prostatitis by two thirds. Sulfathiazole is of definite prophylactic value in preventing complications arising from cystoscopy and ureteropyelography.

*Enuresis.*—Cohen [49] reports the urologic observations in a series of 25 consecutive unselected patients admitted to an army station hospital in the United States because of bed wetting. The following five observations were made:

1. Foreshortening of the trigone was observed in 14 cases. The height of the triangle made by the two ureteral orifices and the internal urethral orifice was diminished. This was the commonest observation. In the course of routine cystoscopy for other diseases, a foreshortened trigone was noted in 2 patients. Neither of these patients had enuresis,

48. Lewis, R. M.: Cystoscopic Reactions, J. Urol. **57**:365-374 (Feb.) 1947.

49. Cohen, D. L.: Nocturnal Enuresis in the Adult Male: A Urological Study, J. Urol. **57**:331-337 (Feb.) 1947.

but questioning revealed that they had both been bed wetters until the age of 15 and 16 years respectively.

2. Hypertrophy of the proximal portion of the verumontanum, that is, the part nearest to the internal urethral orifice, was noted in 13 cases. This was not due to inflammation. The mucous membrane was of normal color and was not injected.

3. Elevation of the inferior margin of the internal urethral orifice was noted in 11 cases. This was not hypertrophy of the median bar of the prostate nor was it an obstruction of the vesical neck.

4. An excavation or depression between the internal urethral meatus and proximal end of the verumontanum was observed. This was more accentuated than in the normal state.

5. Paradoxic cystometric measurements were observed in 6 cases. In the course of routine cystometric studies, diminished voluntary vesical pressure was noted. The cystometric curves were normal. Desire to void appeared when between 150 and 200 cc. of urine was present which was within the normal range. Discomfort was encountered when the bladder was distended to hold 400 or 500 cc. of urine, which is the normal average capacity. However, when at this point the patient was asked to exert maximal voluntary detrusor action, the pressure did not rise to more than 45 cm. of water. On the water cystometer used in these experiments, normal maximal voluntary pressure was between 70 and 80 cm. (or more) of water. In this seeming paradox, sensation was unimpaired, but motor power was somewhat diminished.

*Amicrobic Pyuria.*—Hamm [50] states that cases of so-called amicrobic pyuria constitute a small but important group with urinary infections. The disease in these cases differs from the usual type of pyogenic infection in that no organisms can be demonstrated, either by culture or by Gram stain of the urinary sediment, and it does not respond readily or consistently to any of the known forms of treatment.

The symptoms are severe, with sudden onset of dysuria and micturition, as frequently as once every few minutes day and night, with suprapubic pain and terminal hematuria. Cystoscopic examinations revealed a picture of severe diffuse cystitis and a decidedly contracted bladder. One of the constant observations was generalized dilatation of the upper part of the urinary tract.

In Hamm's cases, treatment with oxophenarsine hydrochloride ("nepharsen") resulted in improvement. The sulfonamide drugs and penicillin were ineffectual. Three patients received streptomycin. In general, the results obtained were satisfactory. Streptomycin was given in doses of 160,000 units every three hours for seven days. Two patients apparently recovered after one course; the third patient was decidedly

50. Hamm, F. C.: Amicrobic Pyuria, J. Urol. **57**:226-232 (Feb.) 1947.

improved after the first course; however, the pyuria did not completely clear up until the second course had been given.

The condition is essentially resistant to all forms of treatment. The duration varies from two to nine months. It appears to be self limited to a certain degree. The course is modified and the symptoms relieved by intramuscular administration of streptomycin and intravenous use of arsenicals ("mapharsen"), but in Hamm's experience neither of these agents can be considered a specific cure. Hamm expresses the belief that microbic infections are true infections of the urinary tract, possibly originating in the urethra, ascending in character and probably caused by an ultramicroscopic organism as yet unidentified.

*Azoospermia.*—Michelson [51] reports 146 cases of azoospermia. In 69 cases (47 per cent) of the series, the cause was determined; in 17 (11 per cent) the cause could be determined only unilaterally; in 60 (41 per cent) this factor could not be determined.

The most frequent cause of degeneration of the spermatogenetic cells was cryptorchism, occurring in 12 cases (8 per cent) of the series. Orchitis due to mumps was the inflammatory disease which most frequently caused degeneration of the spermatogenetic tissue. This occurred in 9 cases (6 per cent) of the series.

The disease most frequently causing obstruction of the vasoepididymal duct was gonorrhea. This occurred in 35 cases (24 per cent) of the series.

Absence of the deferens is a frequently overlooked anomaly. Absence of both vasa is reported in 4 cases.

Testicular biopsy is essential in diagnosis and in determining treatment for azoospermia.

Results of medical treatment are poor. Michelson says that only surgical measures have proved successful.

*Sperm Invasion of Epididymis.*—Steinberg and Straus [52] describe a case in which sperm invasion of the stroma of the epididymis and resultant granulomatous inflammation which simulated bacterial infection occurred. Only 3 similar cases have been found in the literature.

In 2 of the 4 cases reported to date, including these authors' case, either primary or secondary degeneration of the epithelial lining of the tubules was observed. The granulomatous part may be formed at the site of the tubule or may develop in the stroma from the invasion of the sperm. A previous attack of epididymitis may be a contributory factor, but in 2 of the cases no history of previous epididymitis and no evidence of damaged epithelium were obtained. In view of the experimental

51. Michelson, L.: Azoospermia: An Analysis of One Hundred and Forty-Six Cases, J. Urol. **57**:512-518 (March) 1947.

52. Steinberg, J., and Straus, R.: Sperm Invasion of the Epididymis, J. Urol. **57**:498-503 (March) 1947.

evidence of the inherent ability of spermatozoa to penetrate the intact mucosa, the possibility of this additional factor in pathogenesis must be considered.

Though the disease clinically closely simulates tuberculous epididymitis, the differentiation is easily made by microscopic examination.

Conservative management is the procedure of choice. The advisability of resection of the epididymis should be determined by the age of the patient, the desire for more children and the degree of disability produced.

*Urinary Antiseptics.*—Adcock and Plumb [53] report the use of streptomycin in the treatment of 11 patients with urinary infections due to gram-negative bacilli which had failed to respond to treatment with sulfonamide compounds or penicillin or a combination of the two.

The 5 patients with infections due to organisms of the Aerobacter group obtained prompt relief of symptoms; pyuria disappeared, and the urine became and remained sterile. These organisms were extremely sensitive to streptomycin in vitro.

The 5 patients in whom Pseudomonas aeruginosa was present alone or in combination with other bacteria experienced relief of symptoms, and pyuria diminished or disappeared. These effects were often temporary, and bacilluria persisted in each case. These organisms were fairly resistant to streptomycin in vitro.

In several instances the strains of bacteria which were isolated after treatment were much more resistant to streptomycin in vitro than were the strains (presumably the same) which had been recovered originally.

These authors conclude that streptomycin promises to be a useful adjunct to other chemotherapeutic agents in the treatment for certain resistant infections involving the urinary tract.

Kleinman, Shearer and Sprinz [54] present their experiences with streptomycin therapy of nonvenereal infections of the urinary tract in 18 cases. Seventeen of the 18 patients had neurogenic bladders, resulting from injuries to the spinal cord. A preliminary study of the bacterial flora cultures from the infected urinary tracts of 42 similar patients showed that the organisms occurred in the following order of frequency: nonhemolytic streptococci, Bacillus proteus, Aerobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Ps. aeruginosa, Staphylococcus aureus and hemolytic streptococci. All but the last two organisms are known to be resistant to penicillin and the sulfonamide drugs. In vitro studies demonstrated a wide variation in sensitivity within each species, but most strains were susceptible to 64 units or less of strepto-

53. Adcock, J. D., and Plumb, R. T.: Streptomycin for Urinary Tract Infections, J. A. M. A. **133**:579-584 (March 1) 1947.

54. Kleinman, A. M.; Shearer, T. P., and Sprinz, H.: Streptomycin Therapy in Urinary Tract Infections, J. Urol. **57**:599-610 (March) 1947.

mycin per cubic centimeter, a level which is readily attained clinically in the urine.

Dosages of 3,000,000 units of streptomycin a day for three days resulted in prompt but temporary sterilization of the urine. Dosages of 1,200,000 units a day, for three days, generally yielded poor results, except in the patient who did not have a neurogenic bladder. The failure of streptomycin therapy of urinary infections in paraplegic patients with neurogenic bladders is attributed to one or more of the following conditions: persistent suprapubic fistulas, urinary calculi, residual urine, repeated catheterization or inadequate dosage. Inadequate dosage or treatment in the presence of conditions predisposing to failure frequently lead to the prompt development of resistance to drugs. Persistent suprapubic fistula, urinary calculi, residual urine or the need for repeated catheterization each constitutes a contraindication to treatment with streptomycin, except when there is fulminant infection or bacteremia or in association with surgical intervention to correct these conditions.

Pulaski and Amspacher [55] made a critical analysis and study of 465 cases of infection of the urinary tract in which patients were treated with streptomycin. Thirty-four per cent of the patients were cured; an additional 21 per cent improved, while the remaining 45 per cent were not benefited.

Seventy-nine per cent of bacteria isolated were gram-negative bacilli, and 21 per cent were gram-positive cocci, a third of them being nonhemolytic streptococci. The authors state that streptomycin has a potent in vitro action on 87 per cent of the bacterial flora encountered.

Best results of treatment with streptomycin are obtained when infections are due to Ech. coli and Aero. aerogenes. Failures are especially frequent when the causal organism is Ps. aeruginosa. There is no appreciable difference in results of treatment in monobacterial and polybacterial infections, provided, of course, that all organisms are susceptible in vitro to streptomycin.

Presence of obstructive calculi precludes a successful chemotherapeutic result. Patients with paraplegia are benefited by streptomycin therapy, although the effects are rarely permanent except in patients with closed urinary systems and automatic bladders. Advanced renal pathologic conditions, undrained abscesses, neoplasms and infections in the prostate gland are causes of failure of streptomycin therapy.

Streptomycin parenterally administered is excreted in high concentrations in the urine, and intramuscular injection is the preferred route.

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55. Pulaski, E. J., and Amspacher, W. H.: Streptomycin Therapy in Urinary Tract Infections, Surg., Gynec. & Obst. **85**:107-112 (July) 1947.

A total dosage of 1 to 2 Gm. of streptomycin per day for three to five days is recommended for treatment for the average infection of the urinary tract due to susceptible organisms. No advantage accrues from the administration of a second course of the drug if the first course has failed to sterilize the urine. Drug fastness is a constant feature in cases in which the prescribed course of treatment has not sterilized the urine.

When bacteria are not inhibited in vitro by a concentration of 16 micrograms per cubic centimeter, the chances of eliminating them by treatment with streptomycin are not good. This suggests that streptomycin acts primarily through the tissues and not through the urine.

Local instillations of streptomycin have proved to be of no value in the authors' experience, but alkalinization of the urine with streptomycin may be advantageous in selected cases.

There is no contraindication to the concurrent use of penicillin or sulfonamide drugs with streptomycin if it is warranted by the clinical and laboratory observations

The percentage of satisfactory results is highest when the requirements of free flow of urine, susceptible organisms and adequate dosage of the drug are met and due consideration is given to the management of the patient as a whole.

Raines [56] discusses the present status of streptomycin therapy. Streptomycin is effective in varying degrees against gram-negative organisms which are not affected by penicillin and the sulfonamide drugs.

Adequate continuous doses are essential; otherwise streptomycin fastness develops. In vitro titration can serve as a guide to accurate dosage, with a trend toward higher doses.

Drainage of pus and removal of stones, tubes, mechanical obstruction and residual urine are necessary to obtain optimal results. Streptomycin is low in toxicity and, with increasing knowledge of its use, should have a bright future in the treatment for urinary infections.

Mulholland,[57] in discussing use of the sulfonamide drugs and penicillin, states that sufficiently prolonged treatment and adequate dosage with penicillin are necessary to prevent relapse and that effective concentration must be maintained in the blood. Effective levels of penicillin usually vary from 0.02 to 0.16 unit per cubic centimeter of blood, and approximately 25,000 units of the drug is required every two hours, when given by mouth, to maintain this level. Intramuscular

56. Raines, S. L.: The Present Status of Streptomycin Therapy, J. Urol. **57**:79-83 (Jan.) 1947.

57. Mulholland, S. W.: The Sulfonamides and Penicillin as of Today, J. Urol. **57**:196-201 (Jan.) 1947.

injection is the method of choice. Prolonged maintenance of effective levels without high peaks may be attained by giving penicillin in combination with yellow wax, peanut oil, or other agents. Penicillin used for nongonococcic urogenital infections gives less impressive results than when it is used for gonococcic infections. It has proved to be useless against the colon bacillus, which accounts for such a large proportion of urogenital infections. The widest application of it is in the coccic infections, especially those of the kidney and the perinephritic space. Oral use of penicillin is effective in gonorrhea, especially forms resistant to sulfonamide drugs. It is doubtful whether adequate concentrations can be attained in the blood for other types of infections.

Pool and Cook [58] state that two important factors must be considered in the management of infections of the urinary tract. The first is the coexistence of other pathologic processes in the urinary tract. It was observed early that the presence of obstruction, tumor, stone or pronounced chronic inflammatory changes in the urinary tract definitely reduced the efficacy of the ketogenic diet in the eradication of urinary infection and that when none of these pathologic processes were present the results of treatment with the ketogenic diet were much better. Exactly the same observations were made when mandelic acid, the sulfonamide compounds, penicillin and streptomycin were used. The other factor is the variation in the results obtained when combating various strains of organisms. This definitely suggests the importance of using various therapeutic compounds in alternate courses if one or another drug fails to eradicate the infection. Of course, it is useless to do this if coexisting pathologic conditions have not been removed first of all.

For the routine treatment of infections of the urinary tract, mandelic acid and the sulfonamide compounds are still the drugs of choice. Penicillin is a great adjunct to treatment, but it has not been the boon which had been hoped for in the ordinary case of nonspecific infection of the urinary tract. Streptomycin produces spectacular results in some cases of resistant infection of the urinary tract, but it cannot be used routinely at the present time. Our studies concerning this drug are incomplete, because the supply has been so limited that it has been impossible to carry out the investigative work that should go along with the study of any antiseptic.

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58. Pool, T. L., and Cook, E. N.: Present Concepts of Treatment of Infections of the Urinary Tract, J. A. M. A. **133**:584-586 (March 1) 1947.

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